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VETERINARY MEDICINE

OCTOBER CONTENTS 1949

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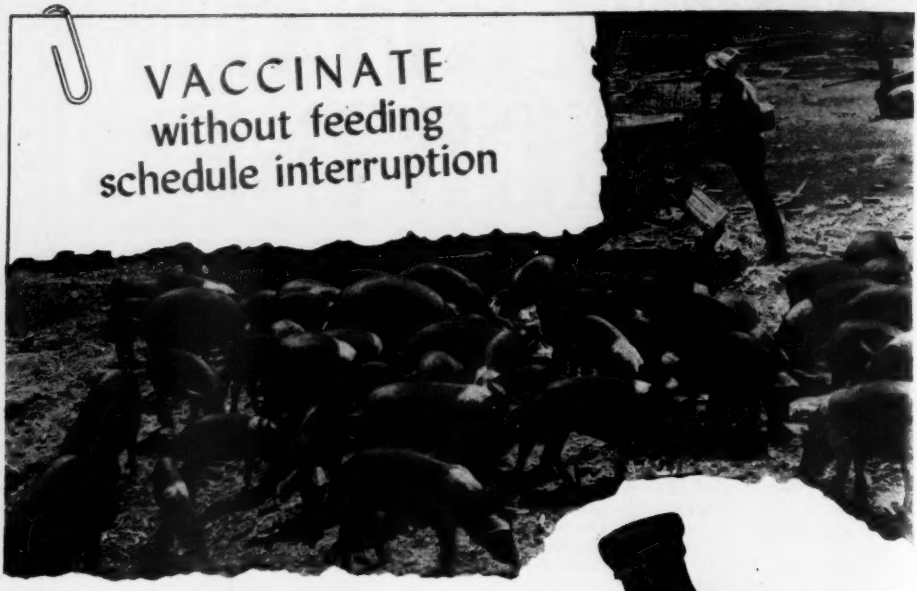

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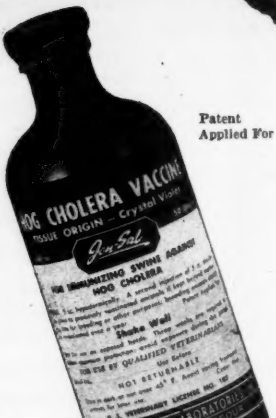

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Inhibition of Lactation in a Bitch

The role of stilbesterol to relieve postpartum engorgement of the breasts and for inhibition of lactation in women is considered rational therapy in human medicine.

Francis Joseph and S. N. Vaidyanathan, *Ind. Vet. Jour.* 25:450 (May), 1949, report the case of a small mongrel bitch that had littered dead puppies two days previously who exhibited painful mammary distention. Stripping the glands of milk and applying a belladonna ointment under bandage failed to effect satisfactory resolution. Two days later the glands were again stripped and 11mg of stilbesterol dipropionate in oil was given intramuscularly. Response to this treatment was spectacular. After 24 hours, only a few drops of altered yellow milk could be milked out which further decreased in the succeeding two days.

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Streptomycin, and streptomycin in combination and *p* aminobenzoic acid, gave good results in the treatment of egg embryos inoculated with various species of Rickettsia, including *R. mooseri,* the cause of Q fever. The combination was more effective than streptomycin alone.—*Jour. Immun., Vet. Bul.* P. 157, April 1949.

The Decision Is Ours

When I was a boy, I thrilled to the recitation of the speech delivered by that revolutionary patriot, Patrick Henry in St. John's Church—as a man I continue to be moved by his words: "I know not what other gentlemen may choose, but as for me, give me liberty or give me death."

Some signs seem ominous. Are we following the road to the destruction of those things we long have held dear? Our profession has most to lose under any other plan than free private practice service.

What can we do? One answer is to exercise our privilege to select those who represent us in our legislative halls. Do you know what per cent of eligible voters cast a vote in your home town, county or state? Was it a majority? We can make our voice heard by registering to vote and voting at every election. If we fail, minority opinions may prevail and we have only ourselves to blame.

A 100% vote will express our wills and 150,000,000 Americans can't be wrong.

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Coprophagy, universally practiced by rabbits, is not a source of coccidiosis infection since "stomach pellets" usually are not sporulated and therefore noninfective.

Veterinary Medicine Under New Editorial Management

With its move to new editorial and publication offices in Kansas City, Missouri, Dr. Robert L. Anderes assumes primary responsibility for the publication of VETERINARY MEDICINE. Dr. D. M. Campbell will continue to contribute to its pages and to the editorial policies, but will not devote his entire time to the work or management detail.

All records, library and equipment have been moved to Kansas City where business pertaining to publication will be conducted. Correspondence in reference to the publication of material, circulation and advertising should be directed to

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Sex Hormones Disappointing in Animals

The use of sex hormones in treating livestock for reproductive troubles is still beset with hazards and difficulties.

There are six reasons why widespread use of hormone products in veterinary medicine is not yet practical.

1. Most of the scientific research has been done with experimental animals, "mainly with white rats."

2. In treating various species of animals, the heredity, environment and many other factors must be considered.

3. Hormones are safely useful only in "selected cases" and "as an aid to other treatment and management practices."

4. The multiplicity of scientific names and trade names for hormones and hormone products is a cause of confusion.

5. The cost of such products often makes it economically impractical to use them.

6. Size and spacing of doses are still experimental problems.—G. H. HART, D.V.M., M.D.

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In the Boston and New York milk sheds, milk production in November and December is only 58% of the production in June. In Toledo, Chicago and New Orleans, production in the low months is 72% and in St. Louis milk shed 77% of the production in May and June. Fluid milk sales are highest in June and lowest in November in all the cities named except Chicago.

Mechanization of Agriculture

At a recent session of the Economic Commission for Asia and the Far East (ECAFE) held in Lapstone, Australia, several delegates from Asia strongly criticized the UN Food and Agriculture Organization (FAO) reports commending mechanization of agriculture.

The Philippine delegate expressed in no uncertain terms that impoverishment followed the importation of American agricultural machinery in the Philippine Islands. This statement may have particular significance as it applies to agricultural practices in all densely populated areas where farming on small holdings is the rule. Considering the matter in terms of food supplies the effort of all concerned is to provide adequate or plentiful nourishing human food. To understand and appreciate the interdependence of agriculture on livestock and *vice versa,* requires the consideration of many basic and intrinsic factors of local or national concern, as the case may be. What may be practical for the great plains area of the United States or the Russian Steppes is not necessarily advantageous elsewhere. It is not altogether a matter of raising "two blades of grass where one has grown," but also to raise a better quality foodstuff mindful of the prime necessity to avoid violation of all elements of soil conservation and the return of fertility to the soil.

Perhaps American agriculture machinery manufacturing interests have been convincing salesmen, but all interests involved should develop a stable recommendation that will insure the results under divergent conditions for which all are striving. Mechanization of agriculture is not a panacea for agriculture's ills, either at home or abroad.

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It may be that many persons do not like cats because of their attitude of independence and indifference, which is quite characteristic in many individuals of all breeds. Others are extremely fond of their feline pets. Cats are seldom demonstrative but are dignified and intelligent animals and reward understanding owners with pleasant companionship. No animal can demonstrate relaxed self-confidence as can the cat. These animals adapt themselves well to all sorts of modern living quarters and are increasing in popularity.

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Pseudocyesis, false pregnancy, is a phenomenon which occurs only in the dog, ferret and rabbit. It is a physiological normal process in the dog.

Artificial Insemination Statistics

Figures compiled by the Bureau of Dairy Industry, USDA, show that there were 316,177 herds, consisting of 2,412,160 cows enrolled as of January 1, 1949, in 1263 artificial breeding associations in the United States. This is an increase compared with figures of a year earlier of approximately 40%.

Wisconsin leads all states in the number of cows in artificial breeding associations with 420,966. New York, Pennsylvania, Iowa and Minnesota follow in numbers in the order given.

This statistical information supports the prophesy of speakers and those who wrote about artificial insemination in dairy cattle ten years ago. At that time there were only six associations organized for this work. The growth has been tremendous. Ten years ago veterinarians were encouraged to participate in this work but the general lack of interest by practitioners at that time and since has resulted in the bulk of the work now being performed by technicians. It is another example of failing to recognize an opportunity to broaden the field of our professional service. Apparently we continue to procrastinate as evidenced by the appeal of C. S. Rhode, Professor of Dairy Production Extension of the University of Illinois, who spoke before the general assembly of the A.V.M.A. meeting in Detroit. Professor Rhode pointed out that the present large scale practice of artificial insemination has focused attention on the very serious problem of sterility in dairy cattle. "Complete cooperation of veterinarians is needed to help solve this problem," he said.

The entire matter has progressed to a point where the practitioner finds much cattle sterility work done by the technician. We will have to take the responsibility for the situation and at the same time interest ourselves in this important work which is still in the growing stage.

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Foot-and-Mouth Disease Laboratory Site

Locations for the foot-and-mouth research laboratory have now been narrowed down to either Ketron Island in Puget Sound or Prudence Island or Jamestown Island on the east coast. The $25,000,000 authorized, will not be appropriated until next year. It is reported that it will require at least a year more before construction can be started.

Dr. Boley Appointed Illinois Veterinary Clinic Head

Dr. Loyd E. Boley, (K.S.C. '32) associate professor, University of Illinois, College of Veterinary Medicine, has been appointed professor and head of the department of veterinary clinical medicine effective September 1.

He temporarily assumed the responsibility of the department in February upon the resignation of Dr. A. G. Danks who is now at the University of Pennsylvania.

Appointed to the University of Illinois in 1936 as an assistant in veterinary pathology and hygiene, Dr. Boley has been responsible for the veterinary care of the University's livestock and for the inspection of its meat and milk products. He has also been teaching courses in veterinary hygiene to agriculture students.

Dr. Boley was formerly engaged in veterinary practice in Burlingame, Kan. He had also served with the meat inspection division of the U. S. Bureau of Animal Industry in St. Joseph, Mo., and Cedar Rapids, Iowa.

During the war. Dr. Boley served with the 7th medical laboratory assigned to Patton's Third army. He was released from the service in March 1946 as a lieutenant colonel.

Dr. Boley received his veterinary degree at Kansas State College and was the first veterinarian to receive the M.S. degree in veterinary pathology and hygiene at the University of Illinois.

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Officers for 1949-50 of Women's Auxiliary to the A. V. M. A.

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Chairman, House of Representatives: Mrs. Charles Rife, Atlanta, Ga.

Demodectic Mange in Dogs

The life cycle of the Demodex mite is not well known. Practitioners who have had experience in the treatment of local or generalized infestation with this parasite in dogs, realize the inadequacy of present recommendations. The parasite which occurs in different species of host is usually regarded as a distinct species, although there is little morphological differences between them other than size. Authors frequently refer to one species, *Demodex folliculorum,* occurring in man, as infesting the hair follicles and sebaceous glands of several mammalian species.

Skin scrapings of apparently normal skin of dogs often reveal these parasites. The same observation is reported by human dermatologists, so that the question of the demodectic mite being the etiological factor in evident mange is questioned. The only satisfactory answer is when resolution of the gross skin lesions follows topical application of agents designed to kill the parasite. This is frequently difficult at best and instances may be related in the author's experience in which a group of topical agents containing acaricides failed to give permanent relief of symptoms. One case of generalized follicular mange in an English Bull Dog responded to long continued and intensive treatment only to develop the severe symptoms, after several months, that were shown earlier in the course of the disease.

The reasons for this may lie in the location of these minute parasites in the hair follicles and sebaceous glands. Even massage with oily preparations cannot be expected to thoroughly penetrate into the depth or fundus of these skin glands. That these parasites invade even deeper tissue is reported by C. C. Lancaster, in correspondence to *The Veterinary Record,* 61:462 (July), 1949. This note is quoted in part: "I remember several years ago having a yard man who was a Bob Tailed Sheep Dog fancier—the Old English Sheep Dog—and one day he brought to me one of his show bitches which had an area of about four square inches in the middle of the back affected with demodectic mange. He asked me take out the skin of that area to stop the disease from spreading. I had never done such a thing before, but I obliged him. I examined the section carefully and found the mites under the skin in the sound areas. From my examination I came to the conclusion that this mite burrows under the skin and comes to the surface here and there, simulating the moles in the fields, and that consequently treatment was virtually impossible."

Hereditary predisposition to follicular mange has been reported and it would appear from the nature of the infestation and the characteristics of the mite that contact mange was possible and probable. A poor state of general health, malnutrition or the debilitated condition following infectious disease are all reported to influence the course of demodectic mange. Likewise, these same factors may influence development of secondary bacterial invasion of the skin due to the inflammation caused by the parasite, leading to pustular dermatitis. Parasitic migration is responsible for the spread to contiguous areas. Strangely, pruritis is at no point in the disease course a symptom of the mange.

To repeat, that until we learn more about Demodex the results of our treatment cannot be expected to be more than palliative. In some cases at least, topical applications have failed, understandable, if invasion of deep skin or subcutaneous tissue by the parasite actually occurs.

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Control of Ectoparasites on Sheep

In trials conducted at the Wisconsin experiment station it was shown that dusting ewes, prior to shearing, and lambs, with benzene hexachloride powder spray containing 1.0% gamma isomers or with a 1.0% rotenone powder, provided complete control of sheep ked, *Melophagus ovinus,* over a 34-day observation period. Rotenone appeared to be most effective of the two dusting powders tried in preventing reinfestation with ked emerging from the pupae stage.

To check the possibility of off flavors in mutton, palatability tests were made of the meat of animals slaughtered ten days, two weeks and one month after dusting with benzene hexachloride. These taste tests failed to show that taints occurred in the meat of the animals given a single dust application.—DICKE, ROBERT L., *et al, Jour. Agr. Res.* 78:565-569 (June), 1949.

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Of three million cattle in 300,000 herds that were vaccinated for the prevention of foot-and-mouth disease in Germany during the 1941 outbreak, 0.35% acquired the disease, in the main within a short period after vaccination. Vaccination against foot-and-mouth disease is regarded as one of the most reliable of known vaccination methods.—*Bio. Abst.*

Inclusion Bodies in Canine Distemper

The question of a rapid method for the differential diagnosis of distemper in dogs is all-important to the practitioner. The experimental work on the histopathology of distemper and other infectious diseases having similar superficial symptoms, has made signal progress. Much work, both in experimental and in naturally occurring cases, remains to be done to remove possible doubt of the regularity of occurrence of the microscopical lesions.

The classical work on inclusion bodies as diagnostic signs of the presence of a virus disease reported, by eminent pathologists, is monumental but complex in technic. It may be that such diagnostic work will remain in a field restricted to the trained pathologist. When one considers the number of years that the laboratory expert has searched for Negri bodies as the diagnostic signs of rabies, a question is raised as to their value. Some laboratories regularly report positive rabies when Negri bodies are demonstrated but do not depend on negative results for negative diagnosis. The clinical symptoms of disease together with the history are in these instances the final basis of judgment in diagnosis. When the brain of an animal suspected of having rabies is found to be negative for Negri bodies on microscopical examination the pathologist can often demonstrate rabies in such brain tissue by animal inoculation. What happened to the inclusion bodies is an unanswered problem. We are told, in the case of rabies, that they appear only late in the course of the disease. Perhaps this does not hold in all diseases. There is thus room for much investigation work in correlating these histopathological lesions with definite clinical and gross pathological lesions.

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In feeding experiments at the Michigan experiment station, it was shown that when dairy cows were fed alfalfa alone the milk production declined abnormally, but a marked increase in production was obtained by supplementing the alfalfa ration with beet pulp or corn gluten meal. At the Arizona station it was shown that the addition of four pounds daily of dried grapefruit peel to the daily ration of alfalfa increased milk production more than did an equal amount of grain mixture. It was concluded that dried grapefruit peel contains factors which stimulate milk production.

Dr. C. F. Clark Rejoins Michigan State College School of Veterinary Medicine

Dr. C. F. Clark has been appointed Professor of Surgery and Medicine, Head of the Department of Surgery and Medicine and Director of the Large Animal Clinic at the School of Veterinary Medicine of Michigan State College, effective September 1, 1949. He will relieve Dr. C. D. Bryan as Head of the Department of Surgery and Medicine.

Dr. C. F. Clark

Doctor Clark obtained his D.V.M. at Michigan State College in 1929, following which he joined the staff of the Department of Animal Pathology, at Michigan State College, where he remained for the period 1929 to June 1946. In 1946, he was appointed to the office of State Veterinarian of Michigan. He has been very active in the U. S. Livestock Sanitary Association, the A.V.M.A., and the State and local veterinary and livestock organizations.

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The Ontario Veterinary Association is considering a cultural exhibit as an added attraction at its annual meetings. If adopted, veterinarians and their wives will be invited to exhibit examples of their handicraft or hobbies —paintings, wood carvings, photographs, etchings, leather craft, needle work, collections of anything from postage stamps to fishing flies, etc.

Bruner, Edwards, and Doll (*Cor. Vet.* 38: 363-366, (Oct.) 1948) confirm the statement of Schneider and Szathmary (*Jour. Ztschr. f. Immunuitätsf.* 94:465, 1949) that in horses, swine, cattle, and goats, there are seven tissue layers between the maternal and fetal circulations and passive immunity is transferred from dam to offspring only through the colostrum. Sheep possess five tissue layers between the fetal and maternal circulations and transmit nearly all passive immunity to lambs through the colostrum. Dogs have four tissue layers between these circulations and transmit passive immunity through both the placenta and the colostrum. In a fourth group of mammals, including rabbits, guinea pigs, rats, mice and man, but three layers of tissue separate the fetal and maternal circulations and passive immunity is transferred from mother to fetus mainly through the placenta. Therefore, survival is doubtful or unlikely in foals, calves, kids and pigs, that do not obtain a feeding of colostrum within a few hours of birth.

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Burmester of the U. S. Regional Poultry Laboratory at East Lansing, Michigan, reported that sex homones have a direct influence on normal oviposition. Evidence was presented that prolapse may result either from insufficient estrogens or from excess androgens. The effect is apparently brought about by hormonal influence on the ligaments of the oviduct, spread of the pubic bones, size of the cloaca and vent, and the pliableness of the abdomen.

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Allen and Hanbury's Ltd., London, advertise penicillin chewing gum in the *British Medical Journal*. For prolonged local medication in the treatment of Vincent's infection, tonsillitis and other infections due to penicillin-sensitive organisms within the buccal cavity. A package of gum of six pieces, ". . . each containing 5000 i.u. penicillin (calcium salt)", is incorporated in a mint flavored gum base.

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A table scrap diet for the family pet may, at times, be too highly seasoned for proper assimilation by the dog and may lead to inflammation to a degree as to produce inappetence and often serious gastroenteritis.

▼ ▼ ▼

If one sets a good example of cleanliness and order at one's office, clinic or hospital associates will follow the example.

Discoloration of the tongue and the growth of fine hair on the tongue associated with the administration of penicillin is reported in the *Jour. A.M.A.* According to this report the tongue abnormalities return to normal in about one month after discontinuance of the penicillin therapy.

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Experiments conducted at the Fromm Laboratories, Grafton, Wisconsin, have confirmed the original observations of Rubarth that canine infectious hepatitis virus and fox encephalitis virus have common antigenic properties and that they should be considered as the same virus.—Siedentopf, H. A., and Carlson, W. E., *Jour. Amer. Vet. Med. Assn.* 115:119 (Aug.), 1949.

▼ ▼ ▼

Percapita consumption of meat in 1948 was 20 pounds greater than in the pre-war period, 1935-39. This means that we ate 3,000,000,000 pounds more meat last year than we would have consumed at the pre-war rate.

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In a study to evaluate chemotherapy in the control of coccidiosis, Amiya B. Kar, *Ind. Vet. Jour.* 25:390-399 (May), 1949, reports in vitro delay of sporulation of oöcytes of rabbit coccidia. A suspension of crystalline diethylstilbesterol in 3% ethyl alcohol was used in the experimental study.

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Antrycide is an astonishing chemotherapeutic agent. It is without toxic effect on mammals, yet is effective against all species of trypanosomes, even a single treatment is often sufficient to free the animal of the parasites. Even more remarkable, it protects the animal from reinfection for periods varying from four to six months depending upon the species of Trypanosoma.

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When the clinical picture of an ailing cow is hazy the blood picture will often clear it.—W. C. GLENNEY.

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Mean Gestation Periods

Ass 380 days.
Goat 155 days.
Sow 120 days.
Rabbit 30-32 days.
Cat 55 days.
Sheep 150 days.
Bitch 63 days.
Mare 353 days.

Continuous Phenothiazine Therapy For Horses

Part I. Effect on the Worm Parasite*

By A. C. TODD,** Ph.D., M. F. HANSEN,** Ph.D., G. W. KELLEY,** B.S. and Z. N. WYANT,** M.S.

A SURVEY of the first appearance and subsequent course of worm infections in Thoroughbreds in central Kentucky, Todd, *et al.* (1949a,b), resulted in a report on a method of low-level phenothiazine therapy, now employed in the control of strongyle infections. The method is based on a schedule of daily treatment with 2gm doses followed by periods of rest from treatment, *vide supra.*

Occasional reports of serious symptoms and mortalities following administration of phenothiazine in therapeutic amounts conditioned acceptance of the drug in equine practice. The reviews of phenothiazine as an anthelmintic by the Imperial Bureau of Agricultural Parasitology (1942, 1947) indicated that the drug is not tolerated by horses as well as it is by other animals. Certainly by 1945, however, phenothiazine had become the drug of choice for treatment of strongylosis in horses. A standard dose for adult horses had been settled upon as 30gm and for weanlings and yearlings, 15gm.

Administration of phenothiazine in subcurative doses is accepted practice with sheep and beef cattle. Ordinarily phenothiazine is fed *ad lib* in a mixture with salt; no control is retained over the amount of the drug consumed by an individual animal.

Because the Thoroughbred horse is fed individually it had appeared to investigators that this animal was obviously well-suited to receive subcurative, *i.e.,* low-level doses of phenothiazine. And wherein the drug would be fed with a margin of safety in respect to the identification of individual horses which would not tolerate therapeutic doses of phenothiazine. A report of the Chief of the Bureau of Animal Industry (1945), after a series of recommendations on administration of phenothiazine to horses, appeared to have settled on six, 5gm doses, fed at daily intervals, for a complete therapeutic procedure. Other methods of feeding fractional amounts of phenothiazine which appeared in the literature, at least through 1946, were all attempts to introduce the standard therapeutic dose for the purpose of reducing the strongyle infections of individual horses.

That systematic low-level phenothiazine therapy provided for older horses might serve as preventive treatment for foals, appears to have been first recorded in detail by the present authors *ibid.* A preventive method was predicated by Dimock (1947) and later summarized in essentials with observations on horses in the field (1949).

The purpose of the experiment presented in part in this paper was to determine the effect of continuous low-level phenothiazine therapy on the intestinal parasite fauna and on the physical well being of horses. The present paper contains data related to reduction of parasitic infections. Later papers in this series will detail the effects of the therapeutic routine on the horses.

Methods

Twelve horses ranging in age from two to eighteen years were divided into four groups. The first group (I) was composed of a Thoroughbred wobbler stud, six years old, a Thoroughbred wobbler mare, six years old, and a five-year-old light-boned mare. The second group (II) was composed of a two-year-old Thoroughbred filly, a three-year-old Thoroughbred filly, and a three-year-old light-boned filly. The third group (III) was composed of a four-year-old Thoroughbred mare, an 18-year-old Thoroughbred mare, and a six-year-old light-boned mare. The fourth group (IV) was composed of two three-year-old fillies, and one nine-year-old mare; all three horses were light-boned.

The horses were maintained almost entirely in box stalls; practically no pasture was avail-

*The investigation reported in this paper is in connection with a project of the Kentucky Agricultural Experiment Station and is published by permission of the Director.

**Department Animal Pathology, Kentucky Agricultural Experiment Station, Lexington, Ky.

able and when turned out they had access only to a bare lot. The feed consisted of hay and corn-corncob meal until July 1, 1948. After July 1, the diet consisted of hay, oats, and corn.

April 26, 1948, one horse in each of the four groups was drenched with 30gm (therapeutic dose) of phenothiazine. April 27, 1948, each horse was given the first daily dose of phenothiazine. Throughout 1948 and for the 52 weeks recorded in this paper, group I received 0.5gm phenothiazine powder daily on its grain ration. Group II received 1.0gm daily; group III received 2.0gm daily; and group IV received 4gm daily.

April 26, 1948, a manure sample was obtained from each of the 12 horses and examined for eggs of parasitic worms. A second examination of the 12 horses was made May 3, 1948; thereafter worm egg counts of the horses were made at intervals of four weeks.

At the completion of the first year of the test one horse in each group was sacrificed and given complete postmortem examination. A representative collection of the parasitic population in each horse was obtained.

Experimental Findings

The complete record of strongyle worm-egg counts obtained from each of the 12 horses is given in table I.

The presence of worm eggs in the feces of the animals was used as a definitive diagnosis of infection. The egg counts indicated that each animal, with the exception of the 18-year-old mare in group III, carried a considerable worm population at the beginning of the test. The average egg counts for the four groups were as follows: (I) 3107 epg (eggs per gram of feces); (II) 1682 epg; (III) 2463 epg; (IV) 2220 epg. No significance was attached to the ages of the groups of horses and their worm burdens.

The egg counts obtained throughout the experiment were directly related to the amount of phenothiazine received by the groups. There was a decrease in egg count corresponding to the increase in phenothiazine fed (table I). Of 42 examinations made of the three horses in group I, (beginning one week after the test was initiated), 41 (97.6%) were positive for worm eggs. Thirty-two (76.2%) of the 42 samples from group II were positive; 23 (57.1%) of the 42 samples from group III were positive; 15 (35.7%) of the 42 samples from group IV were positive.

The 0.5gm daily treatment reduced the worm population of the group I horses slowly and even permitted increases in early summer and mid-fall. The 1.0gm daily treatment appeared to reduce the worm burden more rapidly than 0.5gm treatment but also permitted rises in egg counts in mid-fall. The 2.0gm daily treatment decreased worm population rapidly and with one exception did not permit a subsequent rise in egg count. The 4.0gm daily treatment was most efficient.

The reduction in number of eggs per gram of feces was accompanied by an apparent decline in the fertility of worm eggs passed by the horses. In arriving at an egg count, the number of eggs counted actually is not the total number present in a gram. Instead a definite fraction of a gram is counted and the number obtained is multiplied by a factor. The factor for the counts in this experiment was ten.

Of 2155 eggs actually observed and counted from group I in the 12-month test interval, 262 (12.2%) were infertile. Of 619 eggs counted from group II, 172 (27.8%) were infertile; 54 (23.7%) of 228 eggs from group III were infertile; and 12 (35.3%) of only 34 eggs observed in samples from group IV were infertile.

The principal criterion of infertility employed for these observations was the absence of cell division within the egg. Perhaps all strongyle species in horses produce eggs which are in at least 4 to 16-cell stages when passed. Other criteria were the absence of an equatorial spot indicating fertilization had occurred, and the even density and lack of organization of the cytoplasm.

At postmortem examination the worm population of the one member of each group sacrificed was also related to the amount of phenothiazine received. Two species of the genus Strongylus were found in each of the four horses. Small strongyle species (cylicostomes) were also observed in each horse. The three-year-old filly from group IV which had received 4gm daily doses of phenothiazine had a single female specimen of *Strongylus vulgaris* in the cecum, and one female specimen of *Strongylus edentatus* in the colon. Between 500 and 1000 specimens of cylicostomes were also present in the large intestine. There were eight bloodworms, immature *Strongylus vulgaris*, in the anterior mesenteric artery and its immediate branches.

The six-year-old mare from group III which had received 2gm daily doses of phenothiazine had 37 adult male and two adult female specimens of *S. vulgaris* in the cecum. There were

two male and one female specimens in the colon. One male *S. edentatus* was recovered in the cecum and there were 18 males and five females in the colon. There was a notable increase in numbers of cylicostomes in the large intestine. Three bloodworms were recovered from the anterior mesenteric artery.

The two-year-old filly from group II which had received 1gm daily doses of phenothiazine had one adult male and two adult female specimens of *S. vulgaris* in the cecum and none in the colon. There were 12 male and 11 female

tion of strongyle infections maintained by the experimental animals probably would not apply to horses at Thoroughbred farms. The data from the 12 experimental animals established the 4.0gm daily dose to be most effective, but this group of horses was housed with more than an equal number of horses not undergoing treatment. The conditions for the test were particularly favorable for the development and survival of infective stages of parasitic worms. No doubt under management where horses are rotated from pasture to pas-

TABLE I.

WORM EGG COUNTS OF HORSES RECEIVING DAILY LOW-LEVEL PHENOTHIAZINE THERAPY

		Strongyle Eggs Per Gram of Feces at Examination On Dates Shown													
Dates		4-26-48	5-3	5-24	6-22	7-19	8-16	9-13	10-11	11-8	12-6	1-4-49	2-1	2-28	3-28	4-22
Group	Horse															
I	*6-yr. s	3650	0	60	1136	200	440	590	2250	500	216	240	48	140	64	320
0.5gm	6-yr. m	3240	1810	560	370	1460	660	310	170	600	320	192	32	340	112	64
	5-yr. m	2430	1280	470	180	200	650	270	570	3450	640	888	48	400	64	96
	group av.	3107	1030	363	562	620	583	390	997	1517	392	440	43	293	80	160
II	*2-yr. f	1600	10	10	40	20	20	110	220	170	8	0	32	0	16	0
1.0gm	3-yr. f	1750	470	20	90	180	120	170	150	90	0	24	0	20	64	32
	3-yr. f	1696	1720	280	110	220	60	270	460	920	70	0	0	0	0	0
	group av.	1682	733	103	80	140	67	183	277	393	26	8	11	7	27	11
III	*4-yr. m	4770	40	0	20	70	30	90	30	160	108	216	0	160	0	144
2.0gm	6-yr. m	2570	840	40	0	40	30	50	20	50	24	0	0	0	0	0
	18-yr. m	50	30	40	0	10	0	10	0	0	0	0	0	0	0	0
	group av.	2463	303	27	7	40	20	50	17	70	44	72	0	53	0	38
IV	*9-yr. m	1400	0	0	0	0	30	0	0	20	0	0	0	0	16	16
4.0gm	3-yr. f	2090	100	0	10	0	60	10	0	10	0	0	0	20	32	16
	3-yr. f	3170	0	10	0	0	0	0	0	0	0	0	0	0	32	20
	group av.	2220	33	3	3	0	30	3	0	10	0	0	0	7	27	17

*Drenched with 30gm phenothiazine 4-26-48 s—stallion m—mare f—filly

S. edentatus in the cecum and 24 males and 18 females in the colon. The cylicostomes were more numerous; as many as 50 were counted on a square inch of mucosa in the colon. There were no bloodworms in the anterior mesenteric artery.

The six-year-old stud horse from group I which had received 0.5gm daily doses of phenothiazine had 17 male and 29 female specimens of *S. vulgaris* in the cecum and none in the colon. There were no specimens of *S. edentatus* in the cecum. Fourteen males and 16 females were recovered from the colon. The cylicostomes were extremely numerous; as many were found in the six-year-old stud as in the two-year-old filly from group II. Four bloodworms were recovered from the anterior mesenteric artery.

Discussion

The apparent direct relationship between amount of phenothiazine fed and the reduc-

ture and where one to ten acres are available for each horse the 2.0gm, and perhaps even the 1.0gm, daily dose would be as effective as the 4.0gm doses in this experiment.

The relationship in the equine species between age of host and number of strongyle parasites, reported by Foster (1937), was not considered a factor in the present experiment. Only one aged horse, an 18-year-old Thoroughbred mare, was included with the experimental animals.

The apparent effect of low-level phenothiazine on fertility of strongyle eggs has not been reported previously from experimental horses. The phenomenon has, however, been recorded from horses in the field, Todd and Hansen, (1948).

The number of immature *S. vulgaris* recovered from the anterior mesenteric arteries of the four horses is considered by the present writers to be of significance. A study on the

identity of the causative agent of verminous aneurysm in Thoroughbreds, Todd *et al* (1948), found the larvae to range in number from five to 162 in 20 animals, and average 59. The range for the four experimental horses was zero to eight, and the average was 3.7.

Summary

Four groups of three horses each were fed 0.5, 1.0, 2.0, or 4.0gm of phenothiazine daily for a period of 52 weeks to determine the effect of continuous low-level phenothiazine therapy on the intestinal parasite fauna and on the physical well-being of the horses.

A direct relation was found between amount of phenothiazine fed, the reduction of strongyle infection and prevention of reinfection as evidenced by the number of strongyle eggs passed by the horses.

A relation was also found between amounts of phenothiazine fed and the fertility of worm eggs passed by infected horses.

At postmortem examination of one horse from each of the four groups, a significant reduction in numbers of immature *S. vulgaris* present in the anterior mesenteric artery was found to have occurred.

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Steatitis, yellow fat, in mink has been responsible for large losses in the fur industry. This loss has been due to both mortality early in life, stunted growth in kits that recover, and reduced value of skins because of the lack of coat quality and color. Excellent research on the disease has indicated quite definitely that feeding errors are the responsible factors. This is understandable considering the deviation of modern fur farm feeding practices from those of these animals in the wild state. However, the fact remains that the disease is of relatively recent occurrence, notwithstanding feeding practices, now widely used, are essentially those employed on mink farms since the industry was founded.

The marked and severe symptoms evidenced by the blood picture, the anemia, hemoglobinuria, etc., are so unusual as a result of malnutrition or deficiency disease, that they seem to point to more acute etiological factors, *e.g.,* infection.

Notwithstanding favorable results reported in outbreaks following change of diet and the addition of fresh meats to the ration, experimental study should continue to probe for even more convincing evidence of the etiology of these pathological processes.

▼ ▼ ▼

Antihistaminic treatment gives good results in azoturia and laminitis in horses, in retained placenta and gangrene in cows, and in urticaria, asthma, eczema and edema in dogs.—Rawson.

Biochemists at the University of Wisconsin have discovered a substance in bovine semen that they term "regulator." Its effect is to speed up metabolism in spermatozoa; making them age more rapidly and shortening the period during which they may be used. The discoverers believe if they can find a way to remove this regulatory substance that the practical storage period for semen may be lengthened greatly.

▼ ▼ ▼

Veterinary practice is, first and foremost, a business run for the benefit of the community, but also with strict regard for the future of the principal.—JOHNSON.

▼ ▼ ▼

One of the world's best cows is a 16-year-old Holstein at the Pennsylvania State College which has produced 236,325 pounds of milk containing 7466 pounds of butterfat up to about April 1, 1949. This is over 200 times her weight in milk and approximately equal to ten times her weight in butter.

▼ ▼ ▼

Naturally acquired cases of coccidiosis in rabbits raised on wire or slatted floors are usually subclinical.

Sulfamerazine and Sodium Sulfamerazine as Therapeutic Agents in Cattle

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REMARKABLE advances in the development of chemotherapeutic agents have been made in recent years. Various sulfonamides are of undoubted importance in veterinary practice. The sulfapyrimidine compounds appear to be the most effective and practical derivatives of sulfanilamide for use in the treatment of systemic infections. Sulfamerazine is one of the three sulfapyrimidine compounds in general use at the present time. This drug possesses several very desirable characteristics; including, (1) prompt and marked absorption from the gastrointestinal tract following oral medication; (2) maintenance of effective blood levels for long periods following a single dose; (3) relatively low toxicity when given in therapeutic amounts; and (4) wide range of antibacterial and antiprotozoal activity. These characteristics make it a very desirable compound for use in veterinary practice.

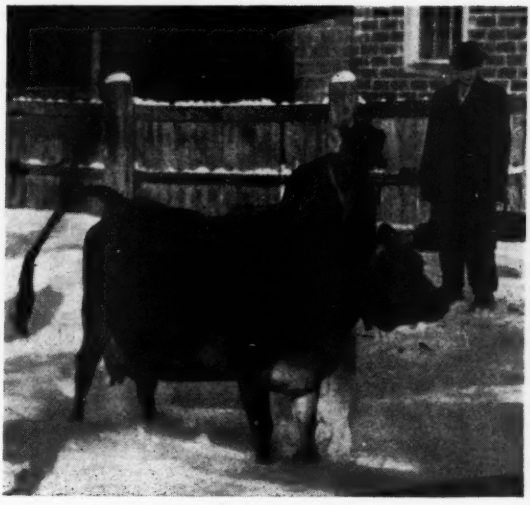
Several reports indicate the value of sulfamerazine in the management of foot rot (fouls) in cattle. Candlin[1] used a dosage schedule of 3gm of sodium sulfamerazine per 100 pounds of body weight, while McAuliff and Phillips[2] usually administered 60gm of sodium sulfamerazine to each adult animal. These clinicians injected the drug intravenously in an aqueous solution. Single doses were effective in a high percentage of the cases. In some cases additional treatment or surgery was necessary to effect a complete recovery.

Thorp[3], Wastrack and Lewis[4], Roberts and Kiesel[5], McAuliff[6], Shaw[7] and Edmonds[8] reported that sulfamerazine is an effective agent for the treatment of several septicemic diseases of cattle.

Sulfamerazine has been demonstrated to be effective also in the control of certain diseases of poultry, such as coccidiosis[9, 12], pullorum disease [13, 16] (in young birds), fowl cholera[17], fowl typhoid [18, 19] and coryza[20].

During the past few years we have had an opportunity to collect clinical data on cases treated with sulfamerazine in general practice (R.H.W.). It has been proved to be a highly useful drug in the management of a variety of infections in animals. This report is a summary of our observations in cattle.

Most of the cases of foot rot are of several days' duration when first seen by us, and are classified as acute or peracute. The animals are lame, the appetite poor, and frequently there is some elevation of temperature. Immediate effective and safe treatment is indicated and, since sodium sulfamerazine meets these qualifications, we have used it intravenously in many cases. We have also given it intraperitoneally to a few cattle. Several animals received sulfamerazine orally in order that blood levels be maintained for long periods.



A variety of infectious diseases of cattle respond promptly to the newer chemotherapeutic agents of the sulfonamide group.

Table I contains information obtained on 17 cases of foot rot treated with sodium sulfamerazine and/or sulfamerazine. Most of the animals in this group (all except three), received sodium sulfamerazine intravenously. Fourteen of the 16 adult animals, that received

TABLE I.—FOOT ROT IN CATTLE TREATED WITH SODIUM SULFAMERAZINE AND/OR SULFAMERAZINE

No.	Animal	Approx. Weight	Treatment	Results	Comments
1	Cow	800	36gm NaSM intravenously	Satisfactory	
2	Cow	1200	36gm NaSM intravenously	Satisfactory	
3	Cow	900	36gm NaSM intravenously	Satisfactory	
4	Cow	1200	48gm NaSM intravenously	Satisfactory	
5	Cow	1200	48gm NaSM intravenously	Satisfactory	
6	Cow	1200	40gm NaSM intravenously	Poor	2nd dose (48gm) given 3 days after 1st treatment (intravenously).
7	Cow	1000	34gm NaSM intravenously	Satisfactory	
8	Cow	1000	36gm NaSM intravenously	Satisfactory	
9	Cow	1000	36gm NaSM intravenously	Poor	
10	Cow	1000	36gm NaSM intravenously	Satisfactory	
11	Cow	1200	40gm NaSM intravenously	Satisfactory	
12	Bull	1500	48gm NaSM intravenously	Satisfactory	
13	Cow	1100	36gm NaSM intravenously	Satisfactory	
14	Cow	1000	48gm SM daily for 4 days	Poor	Drug given orally.
15	Calf	200	6gm NaSM intravenously	Satisfactory	1st day 4gm SM given orally. 2nd day 8gm SM given orally.
16	Cow	1000	36gm NaSM intraperitoneally	Satisfactory	
17	Cow	900	20gm NaSM intraperitoneally	Satisfactory	12gm NaSM intraperitoneally daily for 3 days.

NaSM = sodium sulfamerazine. SM = sulfamerazine.

TABLE II.—OTHER INFECTIONS IN CATTLE TREATED WITH SODIUM SULFAMERAZINE AND/OR SULFAMERAZINE

No.	Animal	Approx. Weight	Diagnosis	Treatment	Results	Comments
1	Cow	1100	Septicemia, mastitis and metritis	48gm NaSM intravenously	Recovered	
2	Cow	1000	Necrophorus infection of skin	36gm NaSM intravenously	Recovered	
3	Cow	800	Actinobacillosis	30gm NaSM intravenously	Recovered	
4	Calf	400	Tendonitis	12gm NaSM intravenously	Recovered	
5	Cow	850	Infected wound	30gm NaSM intravenously	Recovered	
6	Steer	400	Shipping fever	12gm NaSM intravenously	Recovered	
7	Calf	400	Shipping fever	12gm NaSM intravenously	Recovered	
8	Steer	600	Shipping fever	24gm NaSM intravenously	Recovered	
9	Steer	600	Shipping fever	24gm NaSM intravenously	Recovered	
10	Cow	900	Infection of mandible	36gm NaSM intravenously	Recovered	36gm SM orally 2 days
11	Calf	400	Pneumonia	12gm NaSM intravenously	Recovered	12gm SM orally 2 days
12	Cow	750	Diphtheria	24gm NaSM intravenously	Recovered	
13	Calf	200	Pneumonia	6gm NaSM intravenously	Died	
14	Calf	100	Pneumonia	6gm SM orally b.i.d. for 2 days	Improved	
15	Steer	800	Diphtheria	12gm NaSM intravenously	Recovered	
16	Steer	800	Diphtheria	12gm NaSM intravenously	Recovered	
17	Steer	800	Diphtheria	12gm NaSM intravenously	Recovered	
18	Steer	800	Actinobacillosis	30gm NaSM intravenously	Recovered	
19	Cow	850	Actinobacillosis	30gm NaSM intravenously	Recovered	
20	Calf	200	Pneumonia	6gm NaSM intravenously	Improved	
21	Heifer	980	Necrotic vaginitis	30gm NaSM intravenously	Recovered	
22	Cow	1100	Pneumonia	36gm NaSM intravenously	Died	
23	Heifer	750	Actinobacillosis	24gm NaSM intravenously	Recovered	
24	Cow	1050	Pneumonia	36gm NaSM intravenously	Recovered	
25	Bull	1400	Sinusitis	48gm NaSM intravenously	Improved	Local treatment also given
26	Calf	400	Diphtheria	12gm NaSM intravenously	Recovered	
27	Cow	950	Strep. infection of jaw	36gm NaSM intravenously	Recovered	
28	Calf	300	Pneumonia	10gm NaSM intravenously	Recovered	
29	Calf	150	Diphtheria	6gm NaSM intravenously	Recovered	
30	Calf	150	Diphtheria	6gm NaSM intravenously	Recovered	

NaSM = sodium sulfamerazine. SM = sulfamerazine.

20 to 48gm of the drug intravenously or intraperitoneally in a single dose responded satisfactorily, while two did not recover subsequent to treatment. Two of the animals received sulfamerazine orally as maintenance doses. One animal that failed to respond to the treatment received sulfamerazine orally over a period of four days.

A variety of other infections, chiefly pneumonia, shipping fever, diphtheria, and actinobacillosis (pharyngeal region, tongue or jaw) frequently encountered in cattle were treated with sulfamerazine. A tabulation of these cases is given in Table II. In most cases sodium sulfamerazine was given intravenously. The dosage used was approximately 3 to 4gm per 100 pounds of body weight in most animals. Twenty-three of 30 cases listed in this group (Table II) responded satisfactorily to a single intravenous dose of the compound. Three cases received sulfamerazine therapy orally for the maintenance of effective blood levels over extended periods. One of these three animals improved slowly, but the recovery was not entirely satisfactory. These three animals had extremely severe infections. Earlier or prolonged treatment might have produced more favorable results. Two of the 30 animals died within 24 hours after treatment was commenced. These animals received a single intravenous dose of sodium sulfamerazine; however, both had pneumonia and were probably moribund at the time of examination and treatment.

Since sodium sulfamerazine can be given intravenously or intraperitoneally safely and with marked therapeutic effect, it is preferable to use it rather than sulfamerazine since prompt action usually is desirable. Parenteral treatment is particularly desirable in ruminants since oral treatment may result in a delayed absorption of the drug into the blood stream.

Intravenous, as well as intraperitoneal, administration is a surgical procedure that livestock owners appreciate from veterinarians. Subsequent oral use of the sulfonamide in order to maintain effective blood levels may be indicated in some cases. This should not be neglected in severe cases.

Conclusions

Sulfamerazine and/or sodium sulfamerazine has been demonstrated to be beneficial in the treatment of foot rot, shipping fever, pneumonia, diphtheria and actinobacillosis in cattle.

Intravenous injection of aqueous solutions of the sodium salts of the drug provides a convenient method for effective treatment of sick animals.

No toxic reactions were noted following the intravenous, intraperitoneal, or oral administration of the drug to cattle.

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Quinoline Diphosphate in Experimental Anaplasmosis†

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QUINOLINE DIPHOSPHATE alone, and in combination with aricyl, recently has been reported as giving favorable results in acute anaplasmosis[1,2]. The experimental results obtained by the author in a routine checktesting of the anaplasmacidal properties of quinoline diphosphate* and a closely related compound, quinoline phosphate**, may be of interest at this time.

Since these drugs exert a suppressive action on the protozoan organism of malaria it was assumed the action, if any, in the protozoan disease of anaplasmosis would also be of a growth inhibitory nature. Of the many variable factors involved in acute anaplasmosis, Lotze[3] has found the patent rise of infection (rate of erythrocytic infection with anaplasma bodies) to be relatively constant, and he suggests this period be utilized to test anaplasmacidal action of experimental drugs.

The growth inhibitory effects of quinoline diphosphate and quinoline phosphate were determined by therapy during this particular phase of the disease, and the rate of parasitic infection compared to that of untreated cases. The degree of parasitic infection in each case was calculated daily by a count of 500 erythrocytes.

TABLE I.—QUINOLINE DIPHOSPHATE, CALF NO. 1118.

Date	Percentage of Parasitized Cells	Therapy
6-18-48	Anaplasma present	
6-19-48	0.1	
6-21-48	0.4	
6-22-48	1.5	321 mg.
6-23-48	3.4	642 mg.
6-24-48	5.4	642 mg.
6-25-48	8.8	642 mg.
6-26-48	15.8	642 mg.
6-27-48	27.8	642 mg.
6-28-48	34.8	
6-29-48	47.4 (peak of infection)	

†Contribution No. 109, School of Veterinary Medicine, Kansas State College, Manhattan. A cooperative project of the Kansas Agricultural Experiment Station with the U. S. Bureau of Animal Industry.

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*SN 7618-5 (7-chloro-4-(4'-diethylamino-l'methylbutylamino)-quinoline diphosphate), (Dupont).

**SN 13,276-5 (6-methoxy-8-(5'-isopropylaminopentylamino)-quinoline phosphate), (Dupont).

Quinoline Diphosphate

Calf no. 1118, a splenectomized animal, weighing 470 pounds (214kg), showed anaplasma bodies in the peripheral blood on the fourteenth day following experimental inoculation. Table I indicates the progression of the anaplasma infection before, during and after discontinuing therapy. Quinoline diphosphate was administered intravenously at a rate of 3mg/kg/day, one-half the dose every twelve hours. This is at a dosage rate roughly three times greater than that reported by Farley and co-workers[2] as being effective in combination with aricyl. No suppressive action was observed, the number of infected cells being approximately doubled each day. This is a normal rate of erythrocytic infection in acute anaplasmosis as noted by Lotze[3].

TABLE II.—QUINOLINE PHOSPHATE, CALF NO. 1120.

Date	Percentage of Parasitized Cells	Therapy
2-23-49	Anaplasma present	
2-25-49	0.1	
2-26-49	0.7	
2-27-49	1.4	
2-28-49	4.2	775 mg.
3- 1-49	7.0	775 mg.
3- 2-49	11.0	775 mg.
3- 3-49	14.8	775 mg.
3- 4-49	13.6	
3- 5-49	16.4	
3- 6-49	25.2	
3- 7-49	28.6	
3- 8-49	39.0 (peak of infection)	

Quinoline Phosphate

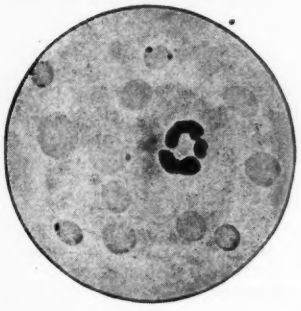
Calf no. 1120: In this experiment anaplasma bodies were observed 28 days after experimental infection. The splenectomized calf, weighing 485 pounds (220.5kg), was treated intravenously at the rate of 3.5mg/kg/day, one-half the dose every twelve hours. Table II, indicates the progress of the infection. The rate of erythrocytic infection was somewhat less than in the previous experi-

ment, but not sufficient to be of any particular significance.

Summary

Quinoline diphosphate and quinoline phosphate showed no evidence of any specific anaplasmacidal action as measured by the patent rise of anaplasma infection. The normal course of erythrocytic destruction followed the peak of infection in each case. The results obtained were not considered sufficiently encouraging to continue additional trials of this nature.

These experiments, although very limited, corroborate the observation by Farley and colleagues[3] that a specific drug for use in anaplasmosis has not as yet been found. Extensive field tests apparently will be necessary before any conclusive evidence can be obtained of the effectiveness of quinoline diphosphate in anaplasmosis.



Anaplasmosis marginale, the causative protozoan organism of anaplasmosis appears as dark staining marginal bodies in the red blood cells. Some authorities regard these bodies as degenerative areas rather than entities.

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Ascites—Prognosis Favorable

By J. DAVID SCHAFFER, B.S., D.V.M.
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UNTIL recently, the diseases of the liver in animals were seldom recognized during life because the symptoms are neither definite nor characteristic[1]. Various theories have long prevailed concerning the etiology of ascites. It is now generally taught that the condition is due, in a large number of instances, to interference with the venous circulation[2]. Any condition which interferes with the peritoneal, portal or mesenteric venous circulation, will cause a collection of serous fluids in the abdominal cavity—ascites. Anomalies such as cirrhosis, neoplasms, tumors or abscesses of the liver are examples. Ascites is frequently a result of failing liver function, rather than a sign of portal stasis[3]. Diagnosis of any of these contributing causes is enhanced by the use of some diagnostic laboratory means[7]. It is imperative that the progressive practitioner apply such a test in every case of ascites presented to him for observation. Early diagnosis of liver damage offers a hopeful prognosis of a once incurable ailment.

In the practice of human clinical pathology, a diagnostic aid known as the Hanger flocculation test to determine liver damage[5] was introduced to the medical profession 10 years ago. This is regarded as an accurate measure of liver dysfunction. It is based upon the principle that cephalin cholesterol emulsion, when properly prepared, is not flocculated by sera from normal individuals, but is flocculated by sera from patients with malfunction of the liver parenchyma. The degree of flocculation parallels the severity of active liver disease, and may, therefore, be employed prognostically in estimating the degree and persistence of the active process[6]. In severe liver damage, a four plus evaluation is observed in six to 12 hours by a complete precipitation leaving the supernatant liquid clear: In moderate involvement or three plus evaluation, the flocculation takes 12 to 24 hours. A slight to moderate deviation from normal is noted by an extended flocculation time of 24 to 36 hours, and a partial or incomplete flocculation. Flocculation requiring 36 to 48 hours is interpreted to mean slight damage. No

pathological change is present if a negative appearance exists beyond 48 hours[7]. The test as applied by this writer in veterinary practice is simple and requires no special equipment. The material[8] used is a modification of that employed in the Hanger test designed for human diagnostic work.

Clinical Report of a Case

April 22, 1949, a male English Setter, five years of age, was presented for treatment. It was quite apparent that the abdomen contained an extremely large amount of fluid. The general condition of the animal indicated that it was suffering from the burden of the heavy fluid; pulse and respiration were increased, gums were pale, eyes dull, together with a general manifestation of anxiety. Nothing in the history shed specific light on the cause. Appetite, bowel condition and urination were normal. Thirst was slightly increased. The client had first noticed the abdominal distention approximately three weeks earlier. The mildly labored heart action was attributed to the weight of the fluid and the effort involved in movement. Urinalysis indicated that apparently the kidneys were normal. There was no pain evidenced on deep abdominal palpation of enlargement. A blood count indicated a slight anemia (4,000,000 RBC per ml). A sample of 10cc of blood was withdrawn from the radial vein for the modified Hanger flocculation test. Five hours elapsed before the first test reading and, at that time, pronounced flocculation (four plus value) was evident. These results justified a tentative diagnosis of hepatitis.

Treatment.—An area on the linea alba, just posterior to the umbilical scar was shaved and an antiseptic applied. Ethyl chloride spray was employed as topical anesthesia. A small incision through the cutaneous tissue was made with a scalpel, and a horse trocar introduced into the abdominal cavity with the animal standing. The muzzled animal offered no resistance. A total of two gallons of clear serous fluid was collected over a period of 40 minutes. The trocar with canula was then removed, but the wound was not sutured. Drainage of a few drops per hour persisted for approximately 24 hours. Instructions were given the client to apply an antiseptic to the drainage area three times daily and to confine the animal in a sanitary pen. Mionine[9], two 0.5gm tablets t.i.d. and bepron elixir[10], one teaspoonful b.i.d. were prescribed.

Two weeks later, the patient was returned for observation, at which time the abdominal muscles had tightened and the abdomen had assumed a normal appearance. No ascitic fluid could be detected by palpation or by mediate auscultation. The gums were healthy pink and the general attitude of the patient was good. A flocculation test gave a reading of one plus at 36 hours which showed a definite tendency toward complete repair. One week later a negative reading was obtained on retest.

Summary

Early diagnosis in ascites may make possible a favorable prognosis in selected cases, when due to liver damage, determined through use of the modified Hanger flocculation test.

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8. Manufactured by Cappel Laboratories, Wayne, Penna.
9. Brand of di-methionine manufactured by Wyeth, Inc., Philadelphia, Penna.
10. A hematinic and tonic manufactured by Wyeth, Inc., Philadelphia, Penna.

▼ ▼ ▼

Rabies in Alaska

Rabies is reported to have reached epizootic proportions in Alaska in 1945-47. Since that time the disease has subsided. The reservoir of infection appears to be well established in Alaskan wildlife, notably foxes and wolves. In foxes the disease manifestations differ from typical rabies in dogs. The furious form is reported to be comparatively mild which may account for the slowness of disease extension in the north country. Many foxes have been reported to approach villages, or attack human beings and their dog teams.

Authentic records are not kept in this vast unsettled country and epidemiological studies present an impossible task. Human infection is significiant because of the common practice to salvage the skins of dead foxes found on the tundra and the lack of effort or means to adequately dispose of carcasses.—WILLIAMS, RALPH B., Epizootic of Rabies in Interior Alaska 1945-47. *Can. Jour. of Comp. Med.* 13:136 (June), 1949.

Demyelinating Diseases of Animals*

Part II. The Relation of Distemper Infection to the Etiology of Canine Encephalopathies

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THE problem of encephalitis in dogs has been inseparably linked with canine distemper and its complexity has revolved around the question: "What are all the manifestations of distemper and how can they be recognized with certainty?" The recent work of MacIntyre, Trevan and Montgomerie[29], is an outstanding milestone in progress, although there is still a long road to travel before we achieve the end. This paper is concerned with the evidence on the potential etiological role of distemper virus infection in the causation of demyelination and encephalitis in dogs. It is written chronologically, to some extent, which will indicate how beliefs have arisen based upon the insecure grounds of clinico-pathological observations alone without resource to good experimentation, and how the lack of irrefutable diagnostic criteria of spontaneous distemper infection in dogs (without resource to ferret inoculation) has hampered progress. It concludes with reference to the work of MacIntyre *et al.*[29] in relation to past history.

The Ancient and Clinical Era

Distemper in dogs was well known more than 100 years ago; in sporting books published about that time distemper may be described and will certainly mention, ". . . the heavy eyes . . . the dry, husky cough . . . the nasty moisture from eyes and nostrils . . . the agitated movements of the limbs so that the dog can barely support himself . . . obstinate purging . . . wasting . . . shivering . . . the endless varieties of the complaint . . ." and last, but not least . . . *"the convulsive fits."* These descriptions are all an elaboration of this theme by veterinarians of that era. Those by Blaine[1] in 1817 and Youatt[48] in 1845 are classical models of shrewd clinical observation and in effect are hardly improved upon in modern veterinary text books.

> The distemper commences its attack in various ways . . . it is a disease that in its rise, appearances, progress, duration and termination exhibits more varieties than any other complaint . . . the first symptom noticed is violent looseness and scowering, in others an occasional fit . . . gradual wasting . . . slight cough . . . nose and eyes become moister . . . watery moisture soon changes to pus . . . eyes and nose glued

Canine encephalitis has been one of the most puzzling diseases of dogs. The etiology given in our literature has often been either vague or controversial; treatment has been hopelessly inadequate and prognosis always grave.

In this scholarly article, Doctor Innes reviews in detail a major portion of experimental work to date on dog convulsions, together with results of his experimental studies, and he classifies in an understandable manner those nervous diseases of dogs that we have been prone to group together.

Doctor Innes has not suggested any schedule of treatment but has prepared a foundation for better understanding of the pathology in nervous diseases in dogs without which satisfactory progress toward relief of these conditions is not possible.

Any practitioner handling dogs has, at one time or another, felt the limitations of the available information about these conditions. This paper will stimulate additional research, and discussion—a better understanding is certain to result.

*Reprinted from *Vet. Rec.* 61:73 (1949) by permission of the editor.

**Doctor Innes is a special Research Fellow, U. S. Public Health Services, Division of Mental Science.

up . . . frequent sneezing, but according as one part or another is the principal seat of complaint so do the symptoms vary . . . appearance of fever is usually considerable . . . dull, disinclination for food, occasional sickness . . . varieties are immense . . . in some an universal eruption on the body under the belly, down inside the thighs . . . eruption is pustular . . . frequently attended by convulsions it is also now and then preceded by them . . . two kinds simple paralytic affection frequently leaves a spasmodic twitching in one or more limbs for life . . . the other is a perfect fit in which every part of the body becomes convulsed . . . attended by mental alienation . . . when distemper has made some considerable progress and fits come on followed in succession by each other the animal seldom recovers . . . fits may appear trifling at first.—Blaine[1].

The stage was thus set for the subsequent traditional belief lasting until now that distemper is a fever with protean manifestations, which in its train might bring exanthematous, gastroenteric, pulmonary and nervous forms. On clinical grounds alone, before the establishment of etiology there was no necessity to dispute this. If there was only one febrile disease of dogs with such a varied clinical picture in different animals, then diagnosis was easy and it was not considered peculiar that some dogs should show severe nervous dysfunction and others should not. (One might draw here the analogy in modern medicine of that vague entity, the flu, with its running nose, red streaming eyes, cough, fever, headache, etc., and postinfluenzal encephalitis.) Pathological contributions on distemper were of little worth, mainly subscribed to what was clinical fact, and were largely observations on pathological anatomy made by clinicians. There were in fact no diagnostic lesions described.

The Etiological Era

The highly infectious and contagious nature of distemper was recognized more than 100 years ago and a form of Jennerian vaccination to create immunity had some vogue. The original identification of the virus nature of the infection was made by Carré in 1905, but final clarification came from the classical contributions of Dunkin and Laidlaw[6] in 1926. This work was done under rigorously controlled conditions; as a start, dogs were bred under quarantine for experimental use. Some of their observations have a cogent importance to the problem of canine encephalitis and some attention thus must be given to what was observed by them. Distemper, as seen by Dunkin and Laidlaw in experimental dogs, was an acute fever beginning after a three to six-day incubation period. The animals showed a diphasic temperature curve, coryza, severe gastrointestinal disturbance with vomiting, loss of appetite, offensive diarrhea and other symptoms due to inflammation of the respiratory tract, while exanthematous rash and transient corneal opacity and keratitis often occurred. Many animals recovered. Nothing characteristic was found at autopsy, not even frank bronchopneumonia, when it was most expected from clinical criteria. This syndrome was seen whether infection was by contact, by intranasal, intracutaneous, or subcutaneous routes and was quite independent of the size of infecting inoculum. In many dogs chorea, fits, and epileptiform convulsions occurred, but there was no pathological substratum to these symptoms in the form of a fulminating encephalitis. In such nervous cases these authors observed only a varied degree of nerve cell damage scattered widely in the brain. They made no claim to have transmitted an encephalitis in the true sense nor to have recovered any neurotropic virus, least of all distemper, from such cases. Under natural conditions, where spread is by contact, we know that the clinical picture is more often complicated by secondary infection and the commonest might appear to be that of pneumonia due to *Bacillus bronchisepticus* and streptococci, etc., or of gastroenteritis. They described the high susceptibility of the ferret to distemper virus and the almost diagnostic course of a coryzal, febrile illness starting after about ten days' incubation which often ended fatally. A small proportion of their experimental ferrets showed nervous symptoms (tremors, twitching, or screaming fits) many of which improved, but although the words, acute encephalitis, are used, they must have been meant in a clinical sense because the lesions were said to be neuronal damage in widely scattered areas of the brain but without inflammatory reaction. (In one ferret which had recovered from distemper, and which was immune to subsequent doses of the virus, an acute encephalitis was found, but the authors frankly acknowledge that perhaps this was due to another infectious agent.) Later, Laidlaw[28] stated that there are no characteristic lesions in distemper and it would be impossible to tell from an autopsy whether or not a dog had died from distemper. "It was the custom to allocate all lesions in the nervous system of dogs to distemper infection, but this could not represent the facts." Further, "brain tissue from severe canine encephalitic cases did not infect ferrets." These are all highly important statements from the workers who originally clarified the etiology of distemper under conditions of experimentation which were rarely fulfilled by subsequent workers.

Many pathologists with an experience of

routine dog autopsy work might differ from these opinions on nonspecific pathology, although Laidlaw no doubt based his views mainly on studies of experimental virus infection. In young dogs, which have suffered from an acute, febrile, coryzal, illness (particularly if the temperature was diphasic) and which on autopsy show a frank bronchopneumonia there might appear to be little doubt of diagnosis from anatomical examination. If sections of nasal mucosa, turbinate bones, bronchial and bladder epithelium in addition showed intracytoplasmic inclusion bodies, a diagnosis of distemper infection might be acceptable to all but the most skeptical. It would seem, however, that there is an urgent need for a complete and thorough reinvestigation of the pathology of distemper* as a whole and not only from the microscopic aspect. Wharton and Wharton[46], considered that distemper was essentially an acute anemia and hypoglycemia. Their paper is noteworthy for the attention paid to clinico-pathological data. The nature, occurrence and distribution of inclusion bodies also requires attention[19]. The work of Kriesel[29], and Watson and Plummer[44], indicate to some extent their variability. The latter consider that inclusion bodies are more likely to be found in an animal in a moribund state than in one at the height of illness and they are an aid to microscopic diagnosis but are not pathognomonic. I have often failed to find cytoplasmic inclusion bodies in so-called typical clinical distemper and have found them when least expecting to find them on the basis of other clinico-pathological findings.

The Pathological Era Without Experimentation

The general belief, starting at least 100 years ago, therefore grew up that an encephalitic form of canine distemper existed although no association with the virus had ever been proved. (A peculiar fact given to me hearsay, to which little attention has been given, emphasized by Bloom [private communication] is that dogs fully recovered from distemper rarely develop encephalitis.) The terms distemper encephalitis, postdistemper encephalitis, distemper chorea, have all been loosely applied to canine cases showing nervous symptoms simply because at one time, or another, the animals had (many had not) suffered from some previous febrile illness which was assumed to be distemper. In view of the lack of knowledge concerning the pathology of canine febrile illnesses this is understandable. Although it seemed that some true canine cases of uncomplicated virus distemper showed nervous symptoms, it is doubtful if any of these had ever shown the same pathologic processes as that seen in a substantiated encephalitis, no matter what type. Yet some veterinary text books, *e.g.* Hutyra, Marek, and Manninger[27], state something to the effect that during the septicemic stage the virus settles in the nervous system where it may cause inflammatory and degenerative processes. The general descriptions in such books would leave one with much perplexity as to the nature of distemper and which would cover a host of manifestations attached to some febrile disorder.

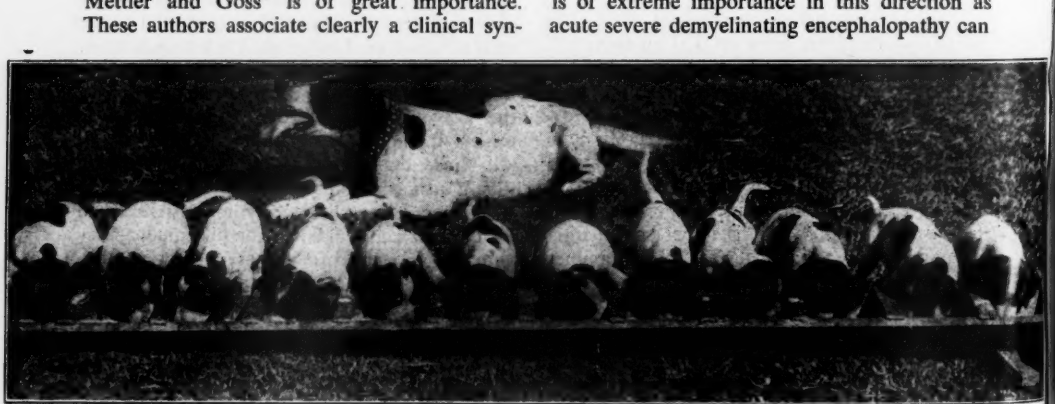
A form of disseminated encephalomyelitis was recognized in the dog by the pathologist long before the isolation of the virus by Dunkin and Laidlaw[6]. One of the earliest papers was that of Cerletti[2] in 1912. A critical analysis of the pathology is made by King and Meehan[26], but it is not the intention to deal with this except in so far as it concerns the connection of the distemper virus with neuropathological findings. The principal features described by those older writers, such as Cerletti[2], were meningoencephalitis with a varying degree of severity of focal and perivascular infiltration of plasma cells and lymphocytes, hemorrhage, gliosis, and proliferation of vascular adventitial and endothelial cells. All of this in the light of present day knowledge is consonant with a virus encephalitis.

It is recognized that a new position was created by the observation of Perdrau and Pugh[34] when the word demyelination was used for the first time in veterinary pathology. They observed demyelination, of a type said to be seen in subacute disseminated sclerosis in man, in four out of 14 encephalitic cases, and admitted that, if a more detailed examination of the nervous system had been made in the others, it might have been found more often. All those dogs had suffered from a febrile illness, at variable previous periods, little different from those with the symptoms described by Dunkin and Laidlaw[6], for distemper. They came to the conclusion that in canine encephalitis the virus of distemper plays a similar mysterious role to that which certain acute infections of varying etiology of man play in the causation of certain demyelinating diseases. (Laidlaw was unable to recover distemper, or any other virus, by inoculation of brain material into ferrets obtained from some similar cases of Pugh.) Demyelination in canine encephalitis was also decribed by Posrednik[38],

*There are no original papers of any merit dealing with the pathology of distemper and it would seem that most pathological data have been transferred from text book to text book and are mainly anatomical.

Marinesco[20] *et al.*, Peters and Yamagiwa[26], and by King [25], who gave a very complete description of the first case of demyelinating encephalopathy in a dog in the United States. In his case King found wide-spread lesions in optic tracts and chiasma, cerebellum, hippocampal fissure and cord. The paper is of importance in other directions in discussing the process of demyelination which he said must be distinguished from destruction of nerve tissue as a whole. Goldberg and Volgenau[9], before the identification of the virus, examined a large number of cases of nervous distemper, but their work is not wholly a pathological study. It is difficult to separate out entities and they may have been dealing with several distinct diseases apart from demyelination. All the features of canine encephalitis described by previous workers were given in great neuropathological detail by Gallego[8]. Frauchiger and Walthard[7], describe the detailed findings in seven cases of distemper with nervous symptoms, and emphasize that there was a great discrepancy between clinical data and the changes in the brain after pathological examination. It is interesting, however, to note that in these seven cases they distinguished individually brain without lesions, necrosis of basal ganglia, diffuse meningitis, venous hyperemia and edema and encephalomyelopathia. (Cordy[5] describes different types of encephalitic lesions in dogs and divides them into clinical groups. In one group frank inflammatory lesions were present in cases diagnosed clinically as distemper. This paper is noteworthy for the attention given to so-called, "old-dog encephalitis," which was almost strictly perivascular lymphocytic inflammation and which was said to be nontransmissible to ferrets.) The paper of Mettler and Goss[21] is of great importance. These authors associate clearly a clinical syndrome of chorea in a dog with a striocerebellar degeneration in which extensive lesions were found in the caudate nuclei (but not the thalamus, globus pallidus or putamen) and severe loss of Purkinje cells in cerebellum and roof nuclei. This chorea in the sense they use it, may have nothing in common with the so-called chorea of distemper in which no pathological studies seems to have been made. On the other hand, some of these lesions may have been described by others in so-called post-distemper encephalitis. Canine chorea according to Mettler and Goss[21] was a symptom-complex which might be caused by other factors than the distemper virus unless the latter produced two different types of pathology. It must also be remembered that there is a growing conviction that some forms of encephalopathy arise on a nutritional foundation, Smith[28], for example, describes a form of ascending paralysis (first spastic and later flaccid) in experimental dogs due to some vitamin B complex factor (no pathological studies were made).

The most that could have been said by pathological analysis at this stage, would be that encephalitis in dogs occupied exactly the same peculiar position to distemper as the so-called post-infective encephalitides in man to various diseases such as smallpox, measles, chickenpox, whooping cough, and influenza, etc. The occurrence of a demyelinating encephalopathy following smallpox and rabies vaccination is in the same category. The latter occurs also in dogs (von Moczy[22]) and has still to be explained etiologically, *i.e.*, whether due to the primary, original virus, the lighting up of another latent neurotropic virus or the effect of heterologous nervous substance. The work of Kabat, Wolf and Bezer[12], and Wolf *et al.*[31], is of extreme importance in this direction as acute severe demyelinating encephalopathy can



The threat of canine virus diseases is a constant and serious limiting factor in dog breeding. The young animals are frequently infected by diseases of obscure source, and, in the case of those affecting the nervous system, create the most difficult problems.

be produced in monkeys (and guinea pigs, Jervis and Koprowski[22]) by a single subcutaneous injection of heterologous, or homologous, brain emulsion with the aid of adjuvants. Antirabic vaccination encephalitis in dogs can be a very severe disease and is similar to the condition produced experimentally in monkeys.

Personal Investigations

In 1939 nearly 50 dogs had been examined* and a complete pathological examination made. All of these cases had been sent in by veterinary practitioners either dead, or in a terminal stage of illness, and diagnosed as suffering from fits, chorea, hysteria, epilepsy or post-distemper encephalitis. The postmortem examinations were carried out in all cases by the usual routine procedure to exclude any possible extracerebral causes of nervous derangement. No single organ in the body was exempt from attention. The brain and parts of the cord were fixed in neutral-formol-saline prior to further examination except in those cases where portions of the brain were preserved fresh for subsequent ferret inoculation. Sections were made at many levels from the olfactory lobes to the brain stem and stained by routine, and neuropathological methods—some after paraffin embedding, others after celloidin. Many other tissues were taken to provide material for a search for inclusion bodies. For control material there was available sections relating to all organs, of hundreds of dogs suffering from a variety of diseases. In a number of cases blood, spleen, liver or parts of the brain were taken, ground up in sterile saline and inoculated into ferrets for distemper virus identification.** This was done with the invaluable help of my chief, T. Dalling†, who had a lengthy experience with canine distemper related to the production of distemper vaccine, while at the Wellcome Research Laboratories, Beckenham. By 1939, it was obvious that for any further profitable investigative experimental work it was necessary to have dogs bred in isolation, and more important still, adequate facilities for working with infections in dogs and ferrets. This was impossible under the circumstances then prevailing and the work was terminated. However, sufficient material had been gathered on which to base a pathological study of canine encephalitis. At that time, Dr. H. J. Scherer, was working in the Institute Bunge, Antwerp, and had published a paper (Scherer and Collet[41]) dealing with three cases of canine encephalitis. It was agreed that some collaborative effort might be made in dealing with the comparative neuropathology of canine disorders. All my sections, and the remainder of fixed soft tissues were sent to him for preliminary study and were lost in the aftermath of war. Suitable acknowledgment in this direction is made in the monograph of Scherer[42], written before his death. A brief description of the findings was given by Innes[20]. A more detailed summary is given below based on the protocols written at that time. Unfortunately, they cannot be supplemented by illustrations, or by a re-examination of the hundreds of sections made, which would have been invaluable in the light of the work of MacIntyre, Trevan and Montgomerie[29]. The various cases had, at that time, been grouped in the following categories:

1. *Distemper and the absence of pathological states in the brain.*—These included dogs which had shown either a febrile illness (distemper) with fits, or fits without any other apparent illness. Some may have been true distemper, while others may have been examples of true hysteria now thought by some to be caused by a toxic factor in flour subjected to the agene process (Parry[43]). No lesions were found in the nervous system. In one case with a history of distemper, ferrets inoculated with spleen/blood emulsion died from a distemper virus infection at the recognized period. There were no visceral lesions present in any of these dogs apart from the occasional case of acute bronchopneumonia.

2. *Distemper and glial clusters in the nervous system.*—In three cases with a history of a recent acute febrile illness (distemper), showing mild fits, glial clusters, (as are seen in many toxemic conditions in man), were found scattered in all parts of the brain. There was no intracerebral inflammatory reaction and no visceral lesions were present.

3. *Distemper and Meningitis.*—In two cases with clinical distemper (a diaphasic temperature curve, great irritability, tremors, fits, one with corneal opacity) there was a mild lymphocytic meningeal infiltration, mainly basal, without involvement of nervous tissue.

4. *Disseminated demyelinating encephalomyelitis.*—By far the largest group of dogs came within this category. The lesions were comparable to those described by many auth-

*Many cases were examined in subsequent years but are not included because of the extremely confusing pictures; one outbreak of distemper I am sure included both distemper proper and some other infection, in different dogs in the same kennel.

**Some of the material at that time was also sent to the Wellcome Research Laboratories for ferret inoculation.

†Then Professor of Animal Pathology, Cambridge, now Chief Veterinary Officer, Great Britain.

ors (*e.g.* Cerletti[2], Perdrau and Pugh[24], Peters and Yamigawa[25], King[25], Hurst[10], Scherer and Collet[41]). There was an extremely wide divergence in the severity and distribution of lesions in the different cases. All showed perivascular, and focal lymphocytic and plasma cell infiltration often sharply delimiting foci of demyelination. Many different regions of the nervous system were affected in various cases; cerebrum, basal ganglia, cerebellum, peduncles, pons, optic tracts and chiasma, and of the cord; reticulin proliferation, the presence of *gemästete* glia and gliosis all mentioned by other authors were seen. The age incidence seemed to be beyond puppyhood, but adult dogs of all ages were included in the series. Fever was not a constantly recorded clinical symptom, while the variability of the length of the illness starting only sometimes with a distemper-like attack was a very outstanding feature. The periods ranged from two weeks to three or fourth months. Fits, intermittency of illness, catarrhal symptoms, various pareses, blindness, vomiting and ataxia, all were mentioned in the clinical reports. In some there was a history of an epizootic trend, more than one dog in a kennel being affected. In a few it was mentioned that the administration of distemper antiserum had no beneficial effect. From one dog at least, distemper virus was identified by inoculation of spleen/blood into ferrets, but attempts to identify any virus by inoculation of brain material into ferrets were negative. (In the monograph by Scherer[42] this type of disease is classified as, "die akute multiple Sklerose des Hundes" and he states that this is the commonest canine encephalopathy, no doubt based upon examination of my own material. This name may to some have too close an annotation to disseminated sclerosis in man.)

5. *Cortical proliferative capillaritis*‡—Three cases had a clinical history of a recent acute febrile illness, two had shown fits and one blindness. In each of these there was present an intense vascular proliferation of the small vessels of cortical and subcortical zones of the cerebrum together with marked macroglial reaction. (Two of these animals had purulent conjunctivitis and a terminal acute bronchopneumonia.) This lesion is described by Scherer and Collet[41], (Case 1) as a pure case. In this series it was present along with the type of encephalitis described in (4). From one of these dogs, inoculation of spleen/blood emulsion into ferrets produced an acute distemper-like illness one month later. (Then assumed to be distemper, but it is now evident from recent work that this might have been some other virus.) Inoculation of brain material from another case was negative up to the same period.

6. *Diffuse lymphocytic perivascular encephalitis with sclerosis.*—Four cases in this group corresponded with case 3, described by Schererr and Collet[39] (Case I) as a "pure case". The four cases were all adult (three very old) dogs. In two, there had been a distemper-like illness at least two years previously, with a subsequent periodic, remittent illness, but one always becoming progressively worse, and with fits and paralysis. In one the pathological process was universal throughout the brain, in another, only the white matter was involved, in another the lesions predominated in the grey matter, but not in cerebellum or cord, while in the fourth perivascular lymphocytic infiltration was almost absent. There was diffuse sclerosis in all and in addition a slight degree of internal hydrocephalus. Injection of spleen/blood and brain from one case into ferrets was negative, while from another the inoculation of spleen/blood, but not brain, caused ferrets to go down with a distemper-like illness.

It was concluded that a number of pathological entities occurred in the brain of dogs, suffering from nervous distemper but in which the association with the distemper virus was problematical—"the etiology was more likely to be linked with a virus, or viruses, not yet identified" (Innes[20]). It was by reflection along these lines that we, Innes and Dalling[21] were attracted to the work of Green *et al.* [10, 35], who had studied fox encephalitis in the United States. It is necessary to mention only relevant observations of Green: (1) a severe form of encephalitis occurred in foxes caused by a filterable virus; (2) this virus was distinct from the canine distemper variety, but was transmissible to dogs but not to ferrets; (3) true canine distemper occurs in the fox; (4) in fox encephalitis infection transmitted to dogs by cisternal routes, specific inclusion bodies are found in ependymal and endothelial cells of the nervous system (as opposed to the neuronal and neuroglial inclusions of distemper); (5) highly specific intranuclear inclusions were found also in hepatic cells. Some preliminary experimental work (six dogs) was therefore done in collaboration with Dalling. Our general conclusions based on this, and

‡This lesion has been described before by other workers as part of a general encephalitic process in dogs and reference is made by some to its occurrence in lead, CO & thiophen poisoning. In view of the fact that apparently it can occur alone I felt it deserved being placed in a separate category (for further discussion see Schèrer 1942).

on my own pathological observations recorded above, can be summarized here:

1. Fox encephalitis virus (Green) and distemper virus infections (using Burroughs Wellcome distemper virus) are separate entities. There is no cross immunity in dogs inoculated with either virus subsequent to recovery from the other infection.

2. The clinical picture of fever and catarrhal symptoms are alike in the experimental dogs, but a diphasic temperature curve is seen only in distemper.

3. Fox encephalitis virus injected cisternally into dogs might produce meningitis, ependymitis or an acute encephalitis.

4. The ependymal and intranuclear hepatic cell inclusions were seen in experimental fox encephalitis virus infection in dogs as described by Green.

5. A type of fox encephalitis had been identified by us in foxes in England. In the two cases seen, the pathological picture showed a symmetry and severity of lesion (localized to temporal lobes), never seen in canine encephalitis. There were, however, no records of natural fox encephalitis infection in dogs in England (see later reference to work of Rubarth). In the light of the work of MacIntyre *et al.*, it is most important for such fox cases to be thoroughly investigated.

6. Intranuclear inclusions in hepatic cells were never seen in any of my cases of natural canine encephalitis or in any form of nervous distemper, hence the conclusion (admittedly based on rather slender evidence) that the fox encephalitis virus had no connection with any form of canine encephalitis as we had seen it.

7. In so-called natural cases of distemper, as diagnosed by the practitioner, which had died or were killed in the acute phase, even those showing some slight nervous manifestations, the brain showed no encephalitis, but might show some neuronal damage, and with a mild meningitis or glial clusters widely scattered in the brain. (Such glial clusters are illustrated in many medical textbooks, *e.g.* Wertham and Wertham[46], who state that they have been given an overestimated specific importance in veterinary neuropathology as a whole. It would appear that this may certainly have been so in distemper so far as any relation to nervous symptoms is concerned.)

8. From canine cases of encephalitis which might, or might not, have had a previous febrile background, distemper virus was never recovered by inoculation of brain material into ferrets, although sometimes an infection, assumed to be distemper, resulted when ferrets were inoculated by spleen/blood from similar cases. (This coincides with later observations of MacIntyre *et al.*).

10. Attempts made to transmit encephalitis from dog to dog have not been universally successful (Dalling, Bloom and others, private communications).

11. Inoculation of distemper virus cisternally into dogs produced distemper but not an encephalitis which by itself is the strongest evidence that the distemper virus is not involved. (Now also confirmed by the recent work of MacIntyre *et al.*)

On purely clinical grounds, to make any inference on the role of the distemper virus in canine encephalitis was obviously unjustified. Pathological studies, did not by themselves help to disentangle the problem because of the variety and severity of conditions found in what was said to be postdistemper encephalitis. Further the pathological evidence indicated that the terms commonly used in a clinical sense, *e.g.* fits, chorea, epileptiform convulsions, encephalitis, and meningitis were vague and meaningless and could rarely be related to what was found pathologically. Controlled experimentation was an obvious need. The few outstanding contributions up to 1948, require some attention because, if anything, they have made matters more perplexing. The lessons learned by Dunkin and Laidlaw had not been taken to heart.

(To be concluded in a subsequent issue in which the references for both this article and the concluding article of the series will be given.)

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Enterotoxemia of sheep, "overeating disease," is caused by *Clostridium perfringens*, an intestinal inhabitant. The disease may be prevented by a bacterin or, temporarily, by an antiserum, which is valuable also as a therapeutic measure.

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Animal sources of protein are exceptionally good ones and, probably for that reason, meat is universally liked. Meat is a source of proteins which supply the essential amino acids as well as generous amounts of iron, phosphorus, thiamine, riboflavin and niacin.

Notes on Veterinary Parasitology

By A. O. FOSTER, B.A., M.A., Sc.D., Beltsville, Maryland

Further Data on Ascaricidal Dosage of Sodium Fluoride for Swine

Extensive experimental and field trials have attested the safety and ascaricidal efficacy of sodium fluoride when given to swine at a level of 1% in dry, ground feed for one day. Although high efficacy has been achieved at somewhat lower dosages, considerable importance, from the standpoint of safety, has necessarily been attached to the self-limited intake of the drug, which obtains when the chemical is fed at the 1% level and to the reflex vomition that occurs in the occasional instances of over-indulgence. In view of the paramount value of preserving these natural safeguards, the question of dosage has been restudied by Dr. F. D. Enzie[1] of the Bureau. In trials with concentrations of 1.0, 0.75, and 0.5% in feed, it was found that the over-all consumption of medicated feed increased when the concentration of the chemical was reduced, but that the amount of sodium fluoride ingested per pound of body weight diminished slightly. It was found also that although the 0.5% level exhibited variable efficacy, the 0.75% concentration of the chemical was as safe and effective as the currently recommended dosage of 1%. At the 0.75% level, however, the decrease in the actual dosage of the chemical was not significant. It was concluded, therefore, that the results did not warrant a reduction in the dosage of 1% currently recommended, but that they revealed the practical advantage of some latitude in dosage. In short, dosage should not exceed 1% sodium fluoride and should not be below 0.75%. Accordingly, convenient modification is permitted in the currently recommended ascaricidal mixture of one pound of sodium fluoride in 99 pounds of dry, ground feed. Safe effective medication results from feeding swine for one day on mixtures of 13 to 16 ounces of technical sodium fluoride in 100 pounds of dry, ground feed. The treatment, as emphasized heretofore in published articles, is contraindicated in gastroenteritis, pregnancy, and lactation.

[1] *Proc. Helm. Soc. Wash.* 16:11-16, 1949.

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Newer Treatments for Demodectic Mange of Dogs

In small animal practice, probably few conditions have been treated with a greater variety of favorite remedies than demodectic mange. Yet, until a comparatively recent date, the treatment of this disease was always tedious and the results frequently disappointing. The prospects of effective, specific treatment brightened considerably with the advent of preparations containing rotenone in oil. The results were sufficiently encouraging to dispel much of the reliance on so-called favorite remedies.

Today, many new and promising treatments are available. Most, if not all, lack extensive experimental and field demonstrations of their efficacy and safety, yet they are certainly deserving of trial when practitioners are confronted with cases of a disease that is so stubborn. Most of the new treatments appear to be comparatively simple to use, as well as effective in the majority of cases. Among those that can be recommended on the basis of published reports are such proprietary remedies as tyroscabe, zylate, and B.L. Emulsion No. 40. The first two contain considerable amounts of benzyl benzoate; the last contains rotenone and a comparatively unknown acaricidal chemical, sodium dihydroxy diphenyl methane. Other medicaments, which are described as effective are colloidal iodine, benzene hexachloride, and chlordane. The first is said to give prompt cures in most cases when applied to affected areas once or twice weekly, and rubbed in until the color disappears. Similarly, cures of red mange have followed two or three local applications, on alternate days of 1% gamma BHC in mineral oil.

In view of recent evidence that demodectic mites may occur in internal tissues and organs, the efficacy of some or all of these new remedies may rest, in part, upon their partial absorption.

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Antigenic Relationship Between Proteus and Brucella in Swine

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IT WAS about the end of 1945, that the author, by chance, noticed the presence of agglutinins of Proteus OX_{19} in the sera of normal swine.

Four samples of swine blood were examined, three of which gave a titer varying between 1:125 and 1:250. The fourth was negative to the agglutination test.

This finding led to the investigation of the prevalence of these antibodies in the blood of normal swine. Samples from 170 hogs were tested for the presence of agglutinins when titrated against a suspension of Proteus OX_{19}. The strain used was no. 3188 obtained from the national collection of culture types, Leister Institute, London.

The results of these agglutination tests are given in table I.

TABLE I.—AGGLUTINATION TESTS OF 170 SAMPLES OF SWINE SERA WITH PROTEUS OX_{19} ANTIGEN IN THE TITER INDICATED.

No. of Cases	1:25	1:50	1:100	1:200	1:400	1:800
13	—	—	—	—	—	—
17	+	—	—	—	—	—
31	+	+	—	—	—	—
57	+	+	+	—	—	—
35	+	+	+	+	—	—
17	+	+	+	+	+	—
Total positives	157	140	109	52	17	0
% Positives	92.1	82.3	64.7	30.5	10	0

From table I, it will be seen that Proteus OX_{19} agglutinins are present in a large number of cases—92.1% of the swine sera examined in dilutions of 1:25 and 1:400. The high titer of the sera tempted the author to investigate the source of these antibodies.

The possibility of these agglutinins being to some extent, nonspecific and of Proteus OX_{19} bearing a serological relationship to organisms belonging to a totally different group has been discussed by various authors. Nicole and Comte[4], were the first to draw attention to the relationship of Brucella to typhus. Kemp, Wright and Wayne, 1933, reported four cases of undulant fever in which various Proteus strains were agglutinated in titers varying from 1:80 to 1:240. These authors stressed the important fact, that there is no increase in the titer as the disease progresses. D. Riding[6], recorded the presence of serological relationship between Brucella and Proteus OX_{19}. Wilson[7], 1934, supported the suggestion, made by certain workers, of the existence of an antigenic relationship between Brucella strains on the one hand and Proteus, Pfeifferella and Pasteurella on the other. Foshay[3], 1940, noted that Brucella antiserum of both horses and goats always agglutinated the O strain of Proteus and almost always all the common organisms, both pathogenic and nonpathogenic, in the intestinal tract of man. His list includes *Proteus vulgaris*, many different strains of colon bacilli, *Eberthella typhosa*, both paratyphoid bacilli and a few other members of the Salmonella group.

Agglutinin absorption experiments were also enlightening in this connection; an untreated Brucella antiserum agglutinated Brucella to titer 1:5120 and Proteus OX_{19} to titer 1:160. After absorption with Brucella, the titer for Proteus OX_{19} the original titer for Brucella, 1:5120, was unchanged. From these experiments, Foshay[3] concluded that these various

The contents of this paper by Doctor Kamel pertaining to cross-agglutination reactions between Brucella and Proteus OX_{19} should be of considerable interest to those who are studying swine brucellosis. Many of the low titer reactions that are now being found in the blood serums of swine in those droves that are free from brucellosis may be due to the presence of Proteus OX_{19} in the swine. It is also possible that similar cross-agglutination reactions occur in the blood serum of cattle not infected with Brucella.—I. Forest Huddleson.

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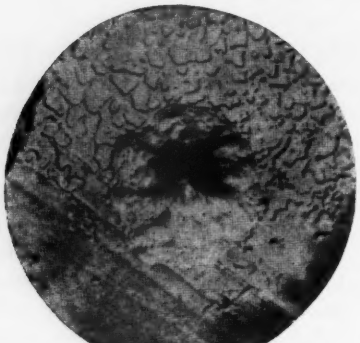
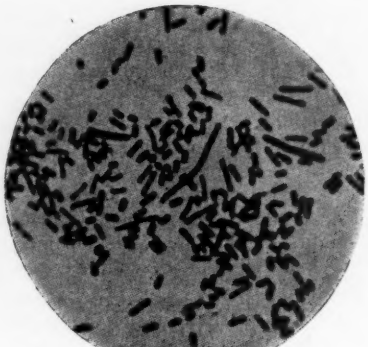
agglutinations were due to the protein nature of the antigenic complex of Proteus OX_{19} and also that Brucella demonstrated a similar complexity in antigenic composition.

Calder[1], 1941, reported the existence of Proteus O and H agglutinins in a large series of patients presumably suffering from chronic brucellosis. Agglutinins for Proteus were frequently noticed in these sick persons. The titers were at times high enough to be interpreted as a positive Weil-Felix reaction. He explains these findings as being due to the presence of an antigenic relationship between Brucella and Proteus, probably due to a certain component shared by the respective somatic antigens.



Proteus vulgaris colony on agar plate showing thin, filmy growth around the main colony.—From *Veterinary Bacteriology*, I. A. Merchant.



Proteus vulgaris from agar culture, X200.—From *Veterinary Bacteriology*, I. A. Merchant.

Dammin and Billings[2], reported that patients infected with *Proteus vulgaris, P. mirabilis* or *Pseudomonas aeroginosa* and who developed appreciable agglutination titers to their own organisms, showed agglutination in significant titers for the Weil-Felix antigens. Sonnenschein[6], reported Preuds-Weil-Felix reaction in patients suffering from septic infections in which streptococci and *P. vulgaris* were isolated from discharges. The sera agglutinated Proteus OX_{19} in dilutions from 1:100 to 1:640. Some of the cases gave a titer of 1:1600. He regarded Weil-Felix titers of less than 1:2000 inconclusive in persons with septic infections unless the symptoms pointed definitely to the diagnosis of typhus. Rickettsial agglutination does not help; being positive in Proteus infections as well as in typhus.

The aim of this work is to determine the specificity or nonspecificity of Proteus OX_{19} agglutinins in swine. The presence of these agglutinins in the blood of swine indicates one of the following possibilities:

1. These antibodies may be, to some extent, nonspecific and are due to the presence of Proteus organisms in the intestines of swine.
2. Proteus OX_{19} may bear some serological relationship to *Brucella suis*.
3. Swine might have been a reservoir of rickettsial bodies owing to an epidemic of typhus that was prevalent in Egypt at the time.

The following materials were examined: (1) Twenty-five samples of swine feces were examined bacteriologically for the presence of Proteus organisms. (2) Samples of swine blood were collected and examined for agglutination against Proteus OX_{19}, somatic antigen of *P. vulgaris* and *Br. suis*. (3) The clots obtained from sera showing high titer against Proteus OX_{19} were inoculated into guinea pigs. After 20 days the guinea pigs were sacrificed and their brains were inoculated into other guinea pigs.

The following technic was adopted: The feces from 25 swine were examined bacteriologically for the presence of Proteus organisms and advantage was taken of the spreading character of the organisms in quickly isolating them in pure culture. This was done by seeding the condensation water of the agar slopes and incubating them at 37°C. After 24 hours the slopes were examined for the spreading growth. From the top of the growth, on the agar slopes, subcultures were made and identified. Using this procedure 19 to 25 specimens of feces examined were positive for

spreading Proteus. All strains gave biochemical reactions of sugar fermentation, characteristic of the organisms, acid and clot with litmus milk and negative indol.

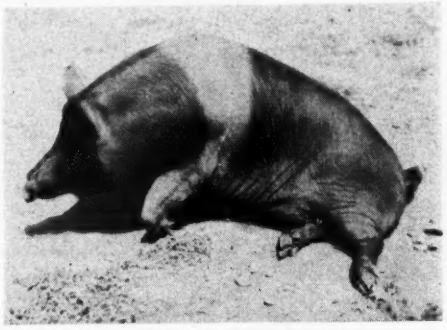
The sera separated from 24 samples of swine blood were titrated against emulsion of Proteus OX_{19}, *P. vulgaris* O isolated from swine feces and against *Br. suis*. The strain of *Br. suis* used was no. 5061 obtained from the national collection of culture type, Leister Institute, London. The opacity of the suspension in every case was equivalent to about a 1000 million organisms per cubic centimeter. Proteus OX_{19} and Brucella were killed by exposure to 60°C. for one hour. Proteus O suspension was prepared by killing the organisms by exposure to 100°C. for one hour. Serial dilutions of the sera; 1:12.5, 1:25, 1:50, 1:100, 1:200, 1:400, 1:800, 1:1600 were prepared, the suspension added and the mixtures incubated at 55° C. for four hours; then left overnight at room temperature before the final reading of the results.

TABLE II.—RESULTS OF AGGLUTINATION WITH 24 SWINE SERA AGAINST PROTEUS OX_{19} PROTEUS AND BRUCELLA

Sera Number	Antigen OX_{19}	Antigen *P. vulgaris* O	Antigen *Br. suis*
1	0	0	1:25
2	0	0	1:25
3	0	0	0
4	1:25	0	1:25
5	1:25	1:25	1:25
6	1:50	1:50	1:25
7	1:50	1:50	1:25
8	1:50	1:50	1:25
9	1:100	1:100	1:100
10	1:100	1:100	1:50
11	1:100	1:100	1:200
12	1:100	1:100	1:25
13	1:100	1:100	1:400
14	1:200	1:200	1:100
15	1:200	1:200	1:200
16	1:200	1:200	1:100
17	1:400	1:200	1:200
18	1:400	1:400	1:400
19	1:400	1:800	1:400
20	1:400	1:800	1:200
21	1:400	1:400	1:200
22	1:400	1:400	1:1600
23	1:400	1:400	1:1600
24	1:400	1:800	1:400

Table II, shows that most of the sera gave a fairly high agglutination titer to the three antigens, Proteus OX_{19}, *P. vulgaris* O and *Br. suis*. It is interesting that the sera which gave a high titer with Proteus OX_{19} also gave a high titer with the other two organisms and *vice versa*. In few instances the titer with Brucella was very high as it reached 1:1600 but did not exceed 1:400 with both Proteus OX_{19} and *P. vulgaris* O.

These findings apparently indicate some serological relationship between Proteus OX_{19}, *P. vulgaris* O and *Br. suis*. It was therefore decided to investigate by animal inoculation whether Proteus OX_{19} shares an antigenic factor with *Br. suis* and the O antigen of Proteus isolated from the feces of swine.



Posterior paralysis in sow associated with *Br. suis* infection of the vertebrae.

Rabbits were repeatedly inoculated intravenously with increasing doses of killed suspensions of *Br. suis*, Proteus OX_{19} and *P. vulgaris* O at weekly intervals and when a satisfactory titer was obtained they were bled and the sera separated and titrated against the homologous organism as well as the other two organisms. The suspensions used for inoculating the rabbit were killed by heating to 60°C. for one hour, except Proteus organism, isolated from the feces of swine, which was killed by heating to 100°C. for one hour, in order to destroy its flagellar antigen. Before inoculating the rabbits, their sera were examined and found to be negative for the presence of agglutinins of the three organisms. Cross agglutination was found to exist between *Br. suis* and Proteus OX_{19} but *P. vulgaris* O stood by itself. (see table III).

TABLE III.—RESULTS OF AGGLUTINATION WITH PROTEUS OX_{19}, *P. vulgaris* O AND *Br. suis* ANTISERUM AGAINST THE THREE ORGANISMS.

	ANTIGENS		
	Proteus OX_{19}	*P. vulgaris*	*Br. suis*
Antisera	titer	O titer	titer
OX_{19}	1:640	0	1:640
Proteus O	0	1:1280	0
Br. suis	1:640	0	1:2560

Absorption tests were then carried out with the organisms apparently sharing, antigenic

factor; Proteus OX_{19} and *Br. suis*, Brucella antiserum was absorbed with a thick suspension of Proteus OX_{19} and Proteus OX_{19} immune serum was absorbed with a thick suspension of *Br. suis*. The mixtures were kept at 37°C. for two hours in the incubator, centrifuged and the supernatant fluid tested on the homologous organism as well as against those used for absorption.

The results of these experiments are seen in table IV and V which shows that Proteus OX_{19} seems to share with *Br. suis* a common antigenic factor.

Table IV.—Result of Absorption of Proteus OX_{19} Antiserum with *Br. suis*.

Bacterial Suspension	1:20	1:40	1:80	1:160	1:320	1:640	Central
Proteus OX_{19}	+	+	+	+	+	+	—
Br. suis	—	—	—	—	—	—	—

Table V.—Result of Absorption of *Brucella suis* Antiserum with Proteus OX_{19}.

Bacterial Suspension	1:20	1:40	1:80	1:160	1:320	1:640	1:2560	1:1280	Central
Br. suis	+	+	+	+	+	+	+	+	—
Proteus OX_{19}	—	—	—	—	—	—	—	—	—

+ = agglutination. — = no agglutination.

The possibility of swine being a reservoir of rickettsial bodies was tested by inoculation of experimental animals (guinea pigs) with swine blood. A good number of guinea pigs were kept under observation for two weeks before the inoculation experiment and their temperatures were noted twice daily, morning and evening, before meals. The animals, which showed a temperature above 39.5°C. were discarded.

Inoculation of Guinea Pigs with Swine Blood for Demonstrating Rickettsial Bodies

Three samples of swine blood which had shown a titer of 1:400 to Proteus OX_{19} were used for inoculation. The clot obtained from 10cc of blood was ground in a sterile mortar with sterile dry sand which had been well washed with acid and then water. When the clot attained the consistency of a paste, 10cc of sterile saline was added and mixed with it and left until the sand and débris had settled. Two male guinea pigs for each sample of clot were inoculated intraperitoneally with 5cc each of the emulsion. The animals were left undisturbed for 48 hours after inoculation, then their temperatures were taken as outlined until the 20th day after inoculation. Not all inoculated animals showed either a febrile response or any local swelling of the scrotum. Temperatures did not exceed 39.4°C. On the 20th day after inoculation all animals were sacrificed. Postmortem examination revealed no pathological changes. Cultures from liver, spleen and heart blood were made. Films were prepared from the tunica vaginalis and stained with Machiavelloe's stain to demonstrate Rickettsia. The cultures and films were all negative.

The brains of the sacrificed guinea pigs were ground with sand as mentioned before and diluted with 30cc of sterile saline. One cc of the brain emulsion was injected intraperitoneally into two other male guinea pigs. The brain of one guinea pig was used for inoculating two other guinea pigs. None of the guinea pigs showed febrile reaction nor local scrotal swelling. The highest temperature was 39.3°C.

Comments

Proteus OX_{19} seems to share an antigenic factor with *Br. suis*. It is agglutinated by *Br. suis* immune serum and can absorb its agglutinins from it as well. *Br. suis* is agglutinated by Proteus OX_{19} immune serum and can absorb its agglutinins from it. The agglutinins against Proteus OX_{19} and Brucella, which appeared in the sera of the swine may be either due to infection of swine with either Brucella or Proteus OX_{19} organisms, but if we bear in mind that swine brucellosis was prevalent when this experiment was conducted, we can safely consider that these agglutinins were due to a subclinical infection with brucellosis.

There is no evidence that these agglutinins were increased either nonspecifically, due to the presence of *P. vulgaris* in the intestine of swine, nor that there is any serological relationship between *P. vulgaris* O and Proteus OX_{19} or *Br. suis*. This is shown by the fact that antiserum against *P. vulgaris* O did not

agglutinate either Proteus OX_{19} or *Br. suis*. At the same time antiserum against Proteus OX_{19} and *Br. suis* did not agglutinate *P. vulgaris* O.

Summary and Conclusions

1. Of 194 swine sera, 178, about 92%, agglutinated Proteus OX_{19} in dilution from 1:25 to 1:400.

2. Of 24 swine sera, 20 agglutinated Proteus OX_{19}, *P. vulgaris* O and *Br. suis* in the following dilution: (a) Proteus OX_{19}, 1:25 to 1:400; (b) *P. vulgaris* O, 1:25 to 1:800; and (c) *Br. suis*, 1:25 to 1:1600.

3. *Br. suis* agglutinins were present in 23 of 24 swine and *P. vulgaris* O agglutinins were present in 21 of the 24 sera.

4. Proteus OX_{19} seems to share an antigenic factor with *Br. suis*.

5. Rickettsial bodies were not present in swine blood which gave a positive Weil-Felix reaction.

6. Proteus OX_{19} antibodies in swine are due, either to infection of swine with this organism or to a latent infection of Brucella, but the prevalence of swine brucellosis in the district when this work was done gives probability that the antibodies against Proteus OX_{19} were due to the serological relationship between Proteus OX_{19} and *Br. suis*.

Acknowledgment

I wish to thank Dr. Zaki Mohamed, Chief Bacteriologist of the Veterinary Pathological Laboratories for his valuable advice and the facilities which he offered me, without which this work would not have been accomplished.

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Deficiency of folic acid in higher animals is characterized by varying degrees of macrocytic hyperchromic anemia, megaloblastic hyperplasia of the bone marrow and leukopenia.—***Scope.***

In Pursuit of Comfort

A 30-year-old mule, when turned out of his stall will invariably go to an old mowing machine that stands in the yard, neatly twist himself around and maneuver into a position so that his belly will rest squarely over the mower wheel as shown in the accompanying

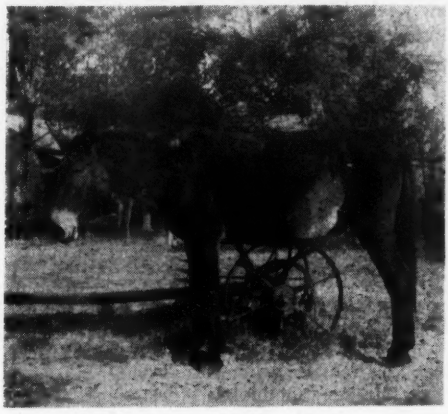

illustration. He has persisted in this habit for several years, remaining in this position for awhile, leaving to graze, only to return to his favorite stand, often remaining motionless for hours. No one has ever given a logical explanation, other than the possibility of the comfort of the position. Perhaps after 30 years he is tired of supporting his belly.

JOSEPH T. ALSTON.

Tupelo, Miss.

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Intravenous administration of 500cc of a 2% formalin solution has been found effective in the treatment of cows secreting bloody milk. G. K. WEIR, Guelph, Ont. *Can. Jour. Comp. Med.*, 13:125-126 (May), 1949.

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Condemnations of beef carcasses for pericarditis at federally inspected meat packing plants totaled 6931 in 1948. The weight of these condemned carcasses was 3,445,000 pounds. Much of this waste could have been avoided by the exercise of care in opening baled hay.

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The Colorado and Illinois departments of health have inaugurated a program among veterinary practitioners for reporting diseases of animals communicable to man.

Comments Upon Animal Health Factors

By R. R. DYKSTRA, D.V.M., Manhattan, Kansas

The vitamin A content of the liver of a calf at birth is at a high level if the cow is fed a ration including vitamin A supplements for a few weeks before calving. Postnatal feeding of this vitamin directly to the calf does not accomplish this purpose.

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Hematologists are interested in typing the blood of twin bovine calves where they consist of a male and a female. There is some early evidence that if the blood samples of the two are identical in blood-type and are composed of a mixture of two kinds of erythrocytes the heifer twin is probably a free-martin. On the other hand if the blood types of the two are different it is assumed that there has been no anastomosis of chorionic blood vessels, and that the female twin will develop normally from the sex standpoint. Anastomosis is the rule—the female being almost always permanently barren.

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The preferred treatment in human medicine for cyanide poisoning consists of amyl nitrite inhalations followed by the intravenous use of a sodium nitrite solution, and finally sodium thiosulfate. This therapy is reported to be several times more effective than intravenous injections of methylene blue. If a high degree of cyanosis develops during treatment oxygen and blood transfusions are given for relief of these symptoms.

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Normally the scrotal region is one of comparatively low temperature. Excessive heat during the summer months or raising temperatures of this region by local heating reduces the vitality of bovine spermatozoa in proportion to the degree of heat applied. This observation in bulls has now been demonstrated experimentally in boars. Holst in Sweden raised the scrotal temperatures of boars by the application of counterirritating ointments and produced a regressive change in spermatogenesis.

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Experience has demonstrated that cattle conceive most readily if, amongst other essential conditions, they are bred late, rather than early, during the estrus cycle—the sperm and ova are most likely to establish the required amalgamation at this stage.

Easley of the Turner Ranch, Sulphur, Oklahoma, who has made an intensive study of bovine artificial insemination, states that; (1) flushing the sheath of old bulls once a week with a normal saline solution reduces bacterial contamination of semen ten-fold, (2) 43°F. is the best temperature for the storing of semen, (3) excessive deposit of fat, especially in the scrotal region, is conducive to low-vitality sperms, (4) that one or at the most two ejaculations a week for dairy bulls used in artificial insemination should be the maximum, (5) that in general the highest percentage of conceptions result from artificial insemination practiced during the spring months—October ranks next, (6) Guernseys show a comparatively low conception rate in artificial insemination statistics.

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Bodin, in the 1947 Collected Papers from the State Veterinary Medical Institute, Stockholm, Sweden, reports on Experiences of Vaccination against Canine Distemper with Virus-Serum according to Laidlaw-Dunkin, and Vaccine according to Green. About 2000 animals were vaccinated by the Laidlaw-Dunkin method and 1400 with the Green vaccine. The investigation showed, "that the risks of inoculation-distemper seemed to be equally great independent of which preparation was used, but immunity attained is better, with statistical significance, after inoculation with vaccine according to Green."

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Weir, in the *Canadian Journal of Comparative Medicine*, emphasizes the use of formalin in controlling capillary hemorrhage in bloody milk in dairy cattle. For many years we have used it in the treatment of petechial fever of horses. For bloody milk, Weir recommends an intravenous injection of 500cc of a 2% formalin solution. To prepare this solution add 10cc of filtered formalin, this is the 37% (approximate) liquor formaldehydi, U. S. P., to 500cc of distilled or tap water provided the latter has been filtered, boiled and cooled. Administer slowly to avoid shock. A second injection three days following the first one is permissible. The solution acts by increasing the thrombin of the blood and the resulting fibrin enmeshes blood elements to form a clot.

Veterinary Problems in Poultry Production

By W. R. HINSHAW, D.V.M., Ph.D., Frederick, Maryland

Effect of High Temperatures On Hens

It is hard to estimate the number of birds that die each year as a result of abnormal air temperatures. In one district in an eastern state last year, 2,000,000 chickens died in a five-day heat wave. Much of the losses from high temperatures can be prevented, according to W. O. Wilson (*Pacific Poultryman*, 53:4, May, 1949), if emergency measures are taken in time. Breeds differ in their resistance to insolation; the White Leghorn appearing to be the most resistant. This may account for the fact they are so popular in hot climates.

According to Wilson, an air temperature of 62°F. is the critical temperature for fowls. Even at 65°F. over a continued period there will be a slight reduction in egg size; at 70°F. egg shells become thinner, and the amount of calcium in the blood is decreased; at 75°F. water consumption is increased, and at 80 to 85°F. the body temperature increases and the heart rate decreases. Panting occurs at 90°F. and egg production falls at this temperature, but fertility and hatchability are not affected until the air temperature reaches 98°F.

When the temperature stays at 100°F. for eight hours or longer, some birds will die, and at 105°F. for four hours or longer the mortality increases rapidly. High humidity aggravates the death rate.

Prevention of losses due to heat, consists in finding methods of cooling the immediate environment of the birds. In some areas sprinkling systems are kept available at all times and are turned on the houses and yards as soon as the temperature reaches the critical point. In extreme cases the litter is sprayed but this may increase the disease hazard. On range, ample shade must be provided. Plenty of cool drinking water, easily available at all times in hot weather, is essential. Since normal feed consumption is cut during hot weather, a supplementary feeding of pellets or wet mash may help to keep the birds in good flesh.

According to Wilson, the best way to revive birds that are overcome by heat is to "dunk" them in water. Care must be taken to prevent drowning, since an unconscious bird may be drowned easily. Plenty of ventilation is necessary, and during the recovery period, it may be desirable to put the birds in a warm spot because during this period the body temperature often drops below normal.

The life of many birds can be saved during heat waves if the owner is alert to see that they are not left too long in the nests. Well ventilated nests will aid in preventing losses. Studying the weather conditions in a particular area so that the temperature for the day may be predicted will aid one in being prepared to care for the overheated flock. In many sections the 9:30 a.m. temperature may be used to predict the daily maximum. If the temperature is 80°F. or higher at 9:00 a.m. one can usually expect afternoon temperatures that will require constant watching of the flock.

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In a review of the information now available on the use of vaccines for prevention of avian pneumoencephalitis Beaudette (*Proc. U. S. Livestock Sanitary Assn.*, 1948:254) states: ". . . only the active (live or modified) virus types fulfill the requirement, namely, that a single infection produces a durable immunity in every bird." Beaudette is a strong advocate of the general use of live virus vaccines, especially in chicken rearing areas that act as supply areas for broiler producers. By such practice the immunized breeding flocks will transmit a parental immunity to the chicks, which will protect them until they can be vaccinated.

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According to Ellis (*Proc. U. S. Livestock Sanitary Assn.* 1948, p.268), the Massachusetts plan for poultry disease prevention emphasizes 10 important points. They are; (1) proper manure disposal, (2) proper dead bird disposal, (3) rodent control, (4) vaccination and inoculation, (5) litter management, (6) rearing replacements away from adults, (7) cleaning and disinfection, (8) proper control of visitors, used crates, feed bags, and egg crates, (9) depopulation and culling, and (10) early correct diagnosis, if disease appears; this often requires a prompt laboratory examination.

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The normal temperature of chickens ranges from 105° to 107°F. When the body temperature reaches 113°F. very few birds will survive. At 110°F. the bird becomes distressed and staggers. The low lethal body temperature for the chicken is 75°F. At this temperature (produced artificially by experimental methods) birds die.

Toxaphene Poisoning: Symptomatology and Pathology

By R. D. RADELEFF,* D.V.M.
Kerrville, Texas

THE quest for organic insecticides comparable in activity to DDT has yielded several new materials. One of these, a material produced by extensive chlorination of terpenes, has been named toxaphene. Its empirical formula is $C_{10}H_{10}Cl_8$. The material has been recommended by its manufacturer for the control of plant-feeding insects. Its use for the control of external parasites of domestic animals is now at the stage of widespread field trial in this and other countries.

Extensive studies of the toxicity of toxaphene were initiated by the Kerrville, Texas laboratory of the Bureau of Entomology and Plant Quarantine as the result of reported field cases of poisoning by the chemical. Preliminary investigations had indicated a wide margin of safety for the material. A complete summation of data accumulated in this and earlier experiments has been published[1 2]. The observations of symptomatology and pathology of poisoning by this chlorinated camphene (toxaphene) reported in this paper were made parallel to the studies of toxicity in the papers noted.

In all cases reported here, the dosage was either applied externally as a spray or dip or given orally as a drench of mixed dip partially to stimulate drinking.

Observations

Case 1.—Goat 3868, oral dosage of 50mg per kg of body weight, was found prostrate two hours after being drenched. Its movements were convulsive, the slightest stimulation increased greatly the intensity of the convulsion. With help the goat was able to stand and walk in an awkward manner for a few steps, then collapsed. At this stage the pulse was 36, the respiration 38 per minute.

Following collapse the goat remained semiconscious for approximately two hours, then was able to stand momentarily. It was discovered, five hours later, quite deliberately and thoroughly butting another goat. When driven off, the animal staggered considerably. Recovery was complete by the next day.

Case 2.—Goat 3806, oral dosage 50mg/kg, was found down and comatose 10½ hours after drenching. When assisted to its feet the goat suffered a severe tetaniform convulsion and remained in a position of opisthotonos until released. Fifteen minutes later it was able to stand and walk, with difficulty, and

The use of toxaphene is extensive in agriculture for the control of plant-feeding pests, particularly grasshoppers. Its use on livestock has not, at this time, been officially recommended by the USDA or the manufacturer. One major dip manufacturer sold an emulsion concentrate in Texas which was extensively used in 1948 for tick and hornfly control at a maximum concentration of 0.55%.

The Bureau of Entomology and Plant Quarantine, in two years of extensive field tests, has found that at 0.5% concentration the insecticide is very effective against ticks and hornflies. Under conditions of severe reinfestation pressure treatments at that concentration have protected the animals against ticks for two weeks and against hornflies for three weeks.

Poisoning could result from ingestion of moderately large quantities of toxaphene on vegetation, from licking containers carelessly disposed of, or from drinking contaminated water or carelessly exposed spray mixtures. In direct applications, poisoning, particularly of young calves, will result if any factor increases the amount of the insecticide deposited on the animal appreciably (2x). Such factors are incomplete emulsification of dips or sprays, break-down of an emulsion or suspension after mixing, careless estimation of water or insecticide quantities or faulty formulation on the part of the manufacturer.

This article has been prepared to give veterinarians advance information which should enable them to diagnose cases of such poisoning should they occur as the use of toxaphene increases.

*United States Department of Agriculture, Agricultural Research Administration, Bureau of Animal Industry, Pathological Division, in cooperation with the Bureau of Entomology and Plant Quarantine.

seemed partially blind. Recovery was complete by the following day.

Case 3.—Goat 3665, oral dosage 100mg/kg, became affected two hours after drenching, evidencing hyperesthesia and salivation, together with tics of the facial muscle groups. It became convulsive two hours later and remained so for 15 minutes. The salivation and nervousness persisted for 24 hours after the disappearance of convulsions. Recovery was complete 48 hours after drenching.

Case 4.—Sheep 3577, oral dosage 100mg/kg, was nervous and apprehensive one hour and 50 minutes after drenching. Ten minutes later it was seized by a brief convulsion, which was repeated after short pauses. Violent paddling, nystagmus, grinding of the teeth, salivation and bleating character-

Typical comatose attitude found in many cases of toxaphene poisoning. On necropsy, increased pressure of cerebro-spinal fluid is noted.

ized the seizures. This sheep died in agony within one hour of the appearance of initial symptoms.

Autopsy: The visible mucous membrane was cyanotic. Drooling saliva had wet the ground under the head and foam was present on the lips. The cecum contained several subserous hemorrhages approximately 8mm in diameter. The remainder of the gastrointestinal tube was normal. The liver, kidneys and lungs were congested. The lungs also showed a few punctate hemorrhages. The heart was in systole and exhibited tiny subepicardial hemorrhages. The brain and spinal cord were congested.

Micropathology: The lungs showed congestion and large amounts of transudate in the alveoli and passages. In the kidneys there was congestion with free blood in and around the tubules. The glomeruli were tightly distended against their capsules. The liver showed only moderate fatty changes and mild congestion.

Case 5.—Sheep 3172, oral dosage 170mg/kg, was found in convulsions three hours after drenching. The clinical symptoms were convulsions, salivation, nystagmus, grinding of the teeth and bleating. The convulsions became milder during the next few hours and recovery was complete 24 hours after the drenching.

Case 6.—Goat 3616, oral dosage 170mg/kg, was affected five hours after drenching. The first symptoms were a staggering gait, muscle tics and salivation. Convulsions quickly followed, being repeated at intervals of 15 minutes to two hours. Between attacks the goat assumed a rigid stance and was oblivious to its surroundings. These symptoms persisted for approximately 36 hours before death occurred.

Autopsy: The body was in a position of opisthotonos. There was bloody froth at the nostrils and foam on the lips. The visible mucous membrane was cyanotic. The small intestine and cecum displayed many small subserous hemorrhages. The stomach was normal. The liver and kidneys were pale. The heart was in systole and showed small subepicardial hemorrhages. The brain and spinal cord were congested.

Case 7.—Sheep 3506, oral dosage 170mg/kg, was affected 5½ hours after drenching, becoming apprehensive and developing muscle tics. Very shortly thereafter it was seized by a convulsion which lasted about 10 minutes. After this single convulsion recovery occurred without further disturbance.

Case 8.—Goat 3642, oral dosage 170mg/kg, was affected five hours after drenching. This animal became weak, staggered, and was either blind or oblivious to its surroundings. This condition persisted for 24 hours and was followed by a short period of convulsions, then the goat returned to a drowsy state. About the 46th hour the goat was reported dead and did indeed seem so, but, when disturbed, it bleated, stood, and walked away. It was found 12 hours later in a highly excited state, which continued for two hours. During the fourth through the ninth days this goat continued to be lackadaisical. Recovery occurred.

Case 9.—Sheep 3809, oral dosage 250mg/kg, became convulsive 2½ hours after drenching. Between convulsions there were severe tremors. The sheep was able to stand 10 minutes later, only to be immediately seized by more convulsions which lasted for an hour. No further convulsions occurred and the sheep recovered. During the convulsions, salivation, crying, grinding of teeth and nystagmus were observed.

Case 10.—Sheep 3814, oral dosage 250mg/kg, staggered and became convulsive two hours after drenching. The convulsion lasted only one minute. A second convulsion occurred one hour after the first. During the next 10 hours of observation the sheep seemed uncomfortable but otherwise was not noticeably affected. Death occurred during the night, some 20 hours after drenching, apparently with the sheep in agony as evidenced by the disturbance of surroundings.

Autopsy: The position of the body was one of opisthotonos. The visible mucous membrane was cyanotic. There was froth on the lips. The cecum, small intestine and stomach displayed small subserous hemorrhages. In the stomach the hemorrhages were particularly numerous in the region of the pylorus. The cut surface of the liver had a "nutmeg" appearance. The liver as a whole was clay-colored. The kidneys were congested. The heart showed vast numbers of very small subepicardial hemorrhages and several diffuse subendocardial ones. The lungs were highly congested. The brain, spinal cord, and the meninges contained an excessive quantity of cerebrospinal fluid. The brain was congested with hemorrhages of the choroid plexuses.

Micropathology: The liver showed no significant pathology in contrast to its gross appearance. In isolated areas fat droplets were observed, some of them completely displacing nuclei. Their paucity suggested normalcy. In the kidneys, there was minor congestion without other significant change.

The spinal cord presented a lacy appearance in

the white matter. The open spaces of this pattern were of a diameter of about 130 microns. In many of these spaces a light-blue staining substance could be seen. In others the material had apparently been washed out. Most of the neurons presented convex margins. In certain areas the neurons appeared somewhat shrunken and the perineuronal spaces enlarged. Many neurons stained diffusely and in such instances the nuclei were barely visible as distinct bodies. In these the cellular outline was one of distention. The meningeal cells appeared swollen.

In the pons the same blue-staining areas were encountered. All the neurons had convex margins.

In the cerebrum the vacuolation was quite marked in the grey matter. The spaces containing the same light-blue-staining substance observed in the spinal cord were, in general, smaller. All neurons presented convex margins and in many the nuclei were undergoing lysis. In many neurons only the nucleoli were distinguishable from the cytoplasm.

In the cerebellum the same general picture obtained as in the cerebrum, but the degenerative changes were not so marked.

Case 11.—Goat 3612, oral dosage 250mg/kg, became highly agitated three hours after the administration, appearing totally blind. A few minutes later it was seized by a convulsive attack which lasted one minute. Immediately thereafter the animal seemed entirely normal and recovered without further event.

Case 12.—Goat 3648, oral dosage 250mg/kg, showed initial symptoms four hours after drenching. Facial tics, apprehension and general nervousness persisted nearly two hours before the animal suffered a convulsion. There were tremors after the convulsion. During the next 12 hours the goat appeared quite uncomfortable. Death occurred during early morning hours, approximately 20 hours after drenching, with the goat in agony as evidenced by disturbance of the area around the carcass.

Autopsy: The position of the body was one of opisthotonos. The visible mucous membrane was cyanotic. There was bloody froth at the nostrils and foam on the lips. Subserous petechial hemorrhages were observed in the cecum and at the pylorus. The liver and kidneys were congested. The heart was in systole. The lungs, brain and spinal cord were severely congested.

Micropathology: The liver showed moderate congestion but otherwise was negative. Congestion of the medullary region was noted in the kidneys. The walls of the convoluted tubules were swollen, their lumina filled with an homogeneous material and occasional clumps of red blood cells.

In the spinal cord there were many light-blue-staining areas and many vacuolated areas unstained, but of identical conformation. Most of the neurons appeared normal. In the grey substance of the cerebrum there were many of the light-blue-staining areas. The neurons appeared unaffected.

There were many of the same light-blue-staining areas in the pons, confined to the outer region. A few neurons showed convex margins. In the cerebellum there was extensive vacuolation, principally of the medullary area. The blue-staining characteristic was confined to the medullary area.

Case 13.—Goat 38, oral dosage 250mg/kg, began staggering two hours after drenching. It was knocked down by other animals and remained in sternal recumbency with the head turned to the flank. Forty minutes later the animal was able to rise but 3½ hours after drenching became convulsive and remained so for an additional four hours until death.

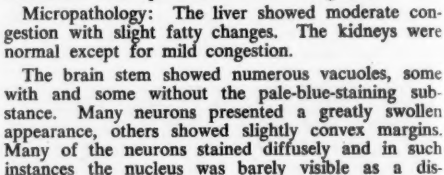
Autopsy: The body was in a position of opisthotonos. The visible mucous membrane was cyanotic. Froth was present on the lips. There were many small hemorrhages along the small intestine. The entire gastrointestinal tract was congested and approximately 250cc of peritoneal effusion was present.

The liver appeared normal. The kidneys and lungs were congested; the passages of the latter contained a bloody froth. The heart was in systole. The brain and spinal cord were congested.

Micropathology: The liver showed moderate congestion with slight fatty changes. The kidneys were normal except for mild congestion.

The brain stem showed numerous vacuoles, some with and some without the pale-blue-staining substance. Many neurons presented a greatly swollen appearance, others showed slightly convex margins. Many of the neurons stained diffusely and in such instances the nucleus was barely visible as a distinct body.

In the cerebrum there was extensive vacuolation as noted for the brain stem. All neurons were rounded. In the cerebellum there was extensive vacuolation of the medullary area. Many of the neurons were rounded. There was moderate congestion.



A sternal position is an attitude frequently assumed by affected animals. This attitude and other symptoms suggest acute distress.

Case 14.—Goat 3622, dipped in an 8% emulsion, became affected three hours after dipping, staggered, showed muscle tics and, finally, was unable to stand. Salivation and muscle tics continued until death the following day, some 30 hours after dipping.

Autopsy: The visible mucous membrane was cyanotic and there was bloody froth at the nostrils. There were subserous hemorrhages in the small intestine. The liver and kidneys were moderately congested but otherwise normal. The heart was in systole and showed numerous subepicardial and subendocardial petechial hemorrhages. There was an excess of pericardial fluid. The lungs were congested and contained a bloody froth in the larger passages. The brain was congested and edematous. The spinal cord was congested.

Micropathology: The liver showed slight fatty changes, congestion and an infiltration of leucocytes.

The kidneys showed only congestion and cloudy swelling. The pons exhibited centrally located blue-staining areas, slight congestion and perioligodendroglial vacuolation. In the cerebrum the perioligodendroglial vacuolation was extensive, there were many blue-staining areas, in the white substance, all small. Neuronophagy was well established. Most neurons were contacted by two or more glial cells. The cerebrum was congested. The cerebellum was congested but there were no blue-staining areas.

Case 15.—Goat 3614, dipped in an 8% emulsion, was affected four hours after dipping, became highly agitated and immediately plunged into severe intermittent convulsions, lying comatose between attacks. Death occurred 1¼ hours later, six hours after dipping. Death was one of agony.

Autopsy: The visible mucous membrane was cyanotic. The body temperature was above 110° F. There was froth at the mouth and rapid bloat occurred, the abdomen being tightly distended 15 minutes post mortem.

There were brilliant subserous hemorrhages, both small and large in size, on the cecum and small intestine. The liver was pale in color, the kidneys normal. The heart was in systole and there was massive subepicardial petechiation. The lungs were severly congested; the parietal pleurae contained hemorrhages.

The brain was congested and edematous; when incised it dripped fluid rapidly. The spinal cord was congested.

Micropathology: The hemorrhages of the intestine noted at autopsy were found to extend from the serosa through the muscular coats to the mucosa. The liver showed moderate congestion with fairly extensive fatty changes, the latter occurring, for the most part, in the central lobular areas.

In the kidneys there was edematous fluid around the glomeruli and tubules. There was congestion with discrete hemorrhages. The tubular epithelium was detached from the supporting structures in many areas. Vacuolation was prominent in the areas of hemorrhage.

There was a fluid exudate in the central canal, otherwise the spinal cord appeared normal. In the cerebrum there was vacuolation. The neurons were rounded, in many the cellular elements were degenerating. The cerebellum was nearly normal, only a few neurons being rounded.

Case 16.—Sheep 3543, dipped in an 8% emulsion, became affected 10 hours after dipping, was at first nervous and agitated, then rapidly progressed to the convulsive state. The convulsions were almost continuous for one hour and 30 minutes, at which time death occurred with the sheep in agony.

Autopsy: The visible mucous membrane was cyanotic and there was blood-tinged froth on the lips. There were a few small subserous hemorrhages in the small intestine, none in the remainder of the digestive tube. The liver was swollen. The lungs were highly congested with free hemorrhage into the larger passages. The heart was in systole and there was multiple petechiation of both the inside and outside surfaces. The kidneys appeared swollen.

Micropathology: The liver showed moderate congestion, cloudy swelling and an excessive number of polymorphonuclear leucocytes. In the kidneys there was congestion of the glomerular tufts. In many instances the capsule of Bowman was detached from its supporting structures. There was congestion of all areas of the kidneys. In the proximal convoluted tubules there were deposits of precipitated or coagulated material. In the lungs, extensive congestion and transudation into the passages, occurred. The cerebellum showed blue-staining areas in the medullary region. There were many oligodendroglial cells showing a narrow peripheral vacuolation.

Case 17.—Goat 3641, dipped in an 8% suspension, was affected three hours after dipping. Profuse salivation and nervousness were the initial symptoms, persisting for 2½ hours and gradually becoming more severe. The goat then suffered convulsions for a short period, after which recovery was prompt and uneventful.

Case 18.—Goat 3669, dipped in a 4% emulsion, became affected eight hours after dipping. The onset of symptoms was very rapid; the goat started to run across the pen, staggered, and fell in a convulsion. Each seizure was severe with only short intervals between seizures. The total time in this condition was approximately one hour, after which the goat appeared dazed, standing motionless and alone. Twelve hours later it was able to walk normally but was still obviously suffering the effects of the seizure. Recovery occurred.

Case 19.—Calf 1, three months of age, sprayed with a 4% suspension, first showed evidence of toxic effect four hours after the application by nervousness and constant walking. These symptoms persisted for the next 15 hours, during which the calf appeared to be blind, walking over other animals and stumbling on small rocks. When at rest the animal stared vacantly at its surroundings. On the morning of the day following application profuse salivation occurred during suckling. Soon thereafter the calf suffered a convulsion. It continued to be affected for a total of 48 hours after spraying. Recovery occurred.

Case 20.—Calf 2, sprayed with a 4% emulsion, became affected 4½ hours later, showing first a nervousness, then continuous, aimless walking. These symptoms continued until the following day when twitching of the facial muscles and nystagmus ensued. There was profuse salivation. When standing, the position of the limbs was awkward. During the afternoon of the second day the calf became convulsive. On the third day after application the muscle spasms ceased but the animal continued to appear stunned by the ordeal. Recovery occurred.

Case 21.—Calf 5, sprayed with an 8% emulsion, two hours later showed salivation and twitching of the facial and body muscles. The calf became convulsive 30 minutes after the onset of the first symptoms. Each convulsion began with a sudden flexion of the limbs, allowing the animal to fall as though shot. During the convulsion the action of the nictitating membranes was remarkable; the movement across the eye being extremely rapid and accompanied by a popping sound audible at a distance of 10 feet. Salivation was profuse and chewing movements pronounced.

Between convulsions, the calf was highly nervous. There was frequent micturition. The final convulsion lasted 15 minutes, the calf dying in agony. The temperature at time of death was above 110° F.

Autopsy: The visible mucous membrane was cyanotic, the globes of the eyes were retracted and the nictitating membranes protruded over half of each eye. There was saliva on the lips. The body was bloated and in a position of opisthotonos.

There were incipient discrete hemorrhages along the intestine and a rather large hemorrhage on the serosa of the pylorus. The intestines were whitish in color. The liver and kidneys seemed normal.

Numerous subepicardial hemorrhages were present closely following the courses of the major coronary vessels. The lungs were filled with air and did not collapse until the trachea was incised.

There was a gush of 5 to 8cc of fluid from the spinal canal as decapitation was performed. The brain appeared to be floating in fluid, was congested and edematous. The spinal cord was similarly affected.

Micropathology: There was moderate cloudy swelling of the hepatic and renal cells. Numerous blue-staining areas were observed in the white substance of the spinal cord. The neurons were swollen, the nuclei pyknotic and the nucleoli were obscure. In the cerebrum there were more of the blue-staining areas and in many areas glial cells were beginning to accumulate around neurons. The cerebellum appeared normal.

Case 22.—Calf 6, sprayed with an 8% emulsion, became convulsive without preliminary symptoms, the first convulsion occurring three hours after spraying and lasting only a minute or two. One hour later the animal was convulsive again, very severely so this time, and was left weakened and obviously stunned. Fifteen minutes later the attack was repeated, initiated by backing, then falling.

Six hours after spraying the most violent attack occurred. The calf leaped high into the air, fell into a fence and tumbled about violently. This turmoil lasted only about three minutes but the animal was unable to stand afterward. Seven hours after spraying, the calf suffered its fifth and final convulsion, dying in agony 20 minutes after the beginning of the seizure.

Autopsy: The body was in a position of opisthotonos, the visible mucous membrane was cyanotic and there was saliva about the face. Some froth was visible at the nostrils.

There were numerous small subserous hemorrhages in the intestine with a large one at the pylorus. There was no enteritis. The liver had a boiled appearance and was clay-colored; no blood flowed from the cut surface. The kidneys were congested. The heart was in systole and the epicardium was showered with petechial hemorrhages. The lungs were moderately congested. Petechiation of the visceral pleurae and the mucosa of the trachea were general. The spleen was normal. The brain and spinal cord were severely congested.

Micropathology: The liver showed mild congestion with leucocytic infiltration. The kidneys showed generalized congestion, distention of the glomerular tufts and free blood cells in the collecting tubules accompanied by a granular precipitate. In the cerebrum there were many blue-staining areas in the white substance. There were perioligodendroglial vacuolation and some neuronophagy. Many of the neurons showed rounded margins. The cerebellum was congested and contained blue-staining areas in the white substance. Many neurons were rounded. In the spinal cord, there were blue-staining areas in the white substance, the neurons were rounded and congestion was evident.

Case 23.—Calf 7, oral dosage 50mg/kg, became affected five hours after drenching. The attack was ushered in with jerking of the head and neck muscles and nystagmus. Convulsion soon followed, the calf remaining recumbent until death 1½ hours later. The convulsions, accompanied by violent paddling, prolapse of the nictitating membranes, grinding of the teeth, profuse salivation, crying and groaning, were almost continuous. The temperature at death was above 110°F.

Autopsy: The body was in a position of opisthotonos. The visible mucous membrane was cyanotic. The nictitating membranes were drawn across the eye balls and there was froth at the mouth. There was marked distension of the abdomen in death.

There were hemorrhages at the pylorus and in the fat posterior to the right kidney. The intestines had a blanched appearance. The liver and kidneys were moderately swollen. The lungs were severely congested and purple in color. There were fibrin clots in the pleural cavity. The brain and spinal cord were congested and edematous. Fluid flowed freely from their cut surfaces.

Micropathology: There was moderate cloudy swelling of the hepatic cells. The kidneys exhibited cloudy swelling of the proximal tubules. The spinal cord showed blue-staining areas throughout the section.

Case 24.—Calf 8, oral dosage 50mg/kg, became disturbed five hours after drenching, showing tics of the facial muscles, twitching of the eyes, and hyperexcitability. These symptoms continued for five hours, after which a pawing movement of the forelegs and a swimming, undulating movement of the body developed.

Recovery was complete by the following day.

Case 25.—Calf 5a, sprayed with a 1.5% emulsion, showed muscle tics and some locomotor interference during the following day. A second spraying was performed at the same concentration four days later, following which the calf died without symptoms having been observed. The ground about the body was disturbed, indicating that the death had been one of agony as had previous similar deaths. The carcass was in a position of opisthotonos.

Autopsy: The visible mucous membrane was cyanotic. The gastrointestinal tube was normal except for some small peritoneal adhesions of long standing. The liver was clay-colored and swollen. The kidneys were normal. The lungs were filled with air; the tracheal mucosa was reddened. The heart was in systole with multiple petechiation of the epicardium and a single diffuse hemorrhage beneath the endocardium.

The brain and spinal cord were congested. There was a hemorrhage at the base of the cerebellum.

Micropathology: The liver showed pronounced cloudy swelling. In the kidneys the proximal convoluted tubules exhibited cloudy swelling while the remainder of the kidneys appeared normal. The cerebrum and cerebellum were congested and the white substance of both showed considerable numbers of blue-staining areas. The blue-staining areas were also present in the grey substance of the spinal cord. There was congestion and most of the neurons were rounded.

Case 26—Calf 12, sprayed with a 1.5% emulsion, showed no toxic reaction to a single application at this concentration, but four days later exhibited nervousness and profuse salivation on the day of a second spraying. The following day this calf suffered a severe convulsion soon after suckling. This was the only convulsion observed and recovery ensued without further event.

Case 27.—Calf 38, sprayed with a 1.5% emulsion, became nervous six hours later, with muscle tics and locomotor disturbances. These symptoms persisted for two hours. A sudden seizure made the animal run across the pen, strike a fence and fall into a water trough. It remained in the trough completely collapsed, for a few minutes, then extricated itself and walked off in a normal manner.

On the following day the calf was drowsy, but uneventful recovery followed. The calf was unaffected by a second application of the same concentration four days later.

Case 28.—Calf 26, sprayed with a 1.5% emulsion, was unaffected by one application. On the day following the second application there were nervousness and salivation. On the following day the calf went into convulsions and died within an hour. There were violent paddling movements, groaning, grinding of the teeth, nystagmus and remarkable activity of the nictitating membranes. Death was in agony. The temperature exceeded 110°F at the time of death.

Autopsy: The visible mucous membrane was cyanotic, there was foamy saliva on the lips and bloat was rapid. The intestines were blanched and contained many subserous hemorrhages. The omentum was showered with small hemorrhages. The kidneys were normal. The liver was clay-colored and firm. Small areas of the lungs were purple-colored and all the lung tissue was hyperemic. The heart was in systole and there were many subepicardial hemorrhages.

The brain and spinal cord were congested. There were hemorrhages at the Circle of Willis and posterodorsally to the cerebellum.

Case 29.—Calf 36, sprayed with a 1.0% emulsion, showed salivation in three hours. Five hours after spraying this salivation became profuse, dyspnea appeared and the calf resorted to open-mouthed breathing. An hour later the animal appeared entirely normal.

The next morning, 20 hours after spraying, the calf was found down, the head pulled back and the mouth twitching. Death occurred a few moments thereafter. The death had been one of agony.

Autopsy: Visible mucous membrane was cyanotic. There was a large quantity of saliva on the ground beneath the head and much froth on the lips. The body temperature one hour after death was in excess of 110°F. The blood vessels of the abdominal cavity were engorged and many petechiae occurred throughout the omentum. The kidneys seemed normal except for slight congestion. The liver showed rounded margins, was clay-colored and splotchy.

The anterior lobes of the lungs were purple-colored, the posterior lobes entirely normal. The heart was in systole. There were numerous subepicardial hemorrhages along the courses of the major vessels. Excessive pericardial fluid was present.

The brain and spinal cord were congested and edematous. Fluid flowed rapidly from their cut surfaces.

Micropathology: The liver showed moderate fatty changes. The kidneys showed only mild congestion and cloudy swelling. The spinal cord exhibited blue-staining areas in the white substance and congestion. In the cerebrum congestion and perioligodendroglial vacuolation were in evidence. The cerebellum showed medullary blue-staining areas and congestion. Many neurons were rounded.

Case 30.—Sheep 3378, 550mg/kg in 50mg/kg repeated oral doses, was being used to build up high tissue residues for chemical and biological study. The sheep was unaffected by the first seven doses but was slightly affected by the eighth (a total of 400mg/kg). Four days' rest was allowed before resuming dosage. The animal suffered convulsions for two hours the day following the ninth dose, recovered and again suffered convulsions after the tenth dose with recovery. The 11th dose proved fatal. The sheep was found dead early in the morning of the day following the 11th dose. The body was in a position of opisthotonos and the ground had been considerably disturbed by the animal's struggles.

Autopsy: The skin and mucous membranes were cyanotic. Foam was present on the lips.

There were many large hemorrhages in the wall of the intestine, extending from the serosa to and through the mucosa. Free blood was present in the lumen of the small intestine. The spleen and kidneys seemed normal. The liver was not swollen but was friable, easily torn by the slightest pressure. The lungs were congested and there were several subpleural hemorrhages. The heart was in systole with many subepicardial hemorrhages.

The brain and spinal cord were congested and edematous.

Micropathology: There was gross fatty change in the liver; hardly a cell that was not filled with either a single large droplet or many small droplets. The change was uniform from the center to the periphery of each lobule. Most nuclei were normal, most cell walls were distended. There was moderate congestion.

In the kidneys pathological changes were principally confined to the cortical area. Here the collecting tubules were swollen, many cells being ruptured. Many nuclei were undergoing lysis; some were pyknotic. The connective tissue was moderately increased. All Bowman's capsules were distended by enclosed precipitated or coagulated fluid. Many hemorrhagic areas accompanied by hemosiderin deposits were present. The medullary area failed to disclose significant changes aside from congestion.

In the spinal cord neuronal changes were evident. There were perineuronal vacuolation, degeneration of neurons, and shrunken cell bodies in many instances.

In the cerebrum there was congestion with polyleucocythemia. In addition there were perioligodendroglial vacuolation and neuronophagy.

In the cerebellum no significant changes aside from congestion were found.

Discussion

From the foregoing descriptions of the symptomatology of individual cases it appears that two distinct syndromes exist, either or both of which may occur in a single case. Some animals react as though stunned, appear blind and fail to feed. In such cases, although the animal performs as though blind it is actually capable of vision. It would thus seem that the stunning and apparent blindness are produced by the depressant effect of the increased pressure of cerebro-spinal fluid rather than principally by neuronal damage. In other cases violence is the most obvious characteristic and seems to be due to specific irritation of the neurons. In many cases it appears that the two etiological factors alternate in production of symptoms with the depressant action being the more constant and the irritative effect breaking over the threshold established by the depressant action. Regardless of the

syndrome observed, it is apparent that toxaphene exerts its acute influence principally through the central nervous system. The gross and microscopic lesions tend to confirm this hypothesis. The petechiation and congestion of various organs are observable in most animals dying in convulsions and are in themselves not pathognomonic; however, the presence of an excessive amount of fluid in and around the central nervous system is more definitive since it is less frequently encountered in routine autopsies.

Significant liver and kidney pathology appears to become evident only if the duration of illness is prolonged or the dosage is administered in small quantities over an extended period. Involvement of the brain and spinal cord occurs very rapidly, as might be expected by the symptoms manifested. Attention should be called to the fact that while two animals may receive identical doses of toxaphene, react in an identical manner and die in the same length of time, the gross and microscopic pathology of the two may, and often does, vary to extremes.

The phrase "blue-staining areas" has been used descriptively throughout this paper. It has been so used since the condition it describes is not at once identifiable. That the areas may be artifacts does not seem likely since the lesions are noted consistently in these cases and not in other nervous tissue processed in identical manner. The most acceptable explanation of the nature of the areas in that they are accumulations of mucin. The picture obtained in the foregoing sections matches that presented by Grinker and Stevens[5] in their discussion of mucoid degeneration of the oligodendroglia and formation of free mucin. Their statement as to the etiological conditions requisite to the phenomenon lists the terminal states such as fever, dehydration, anorexia, anemia and death in agony. All of the above, save anemia, have been noted in poisoning by toxaphene. Pathologists recognize the occasional presence of such material in small quantity in "normal" nervous tissue but never in such large quantities as is to be observed in the sections herein reported.

The word "convulsion" is used throughout this discussion and should be more accurately described. Typically the animal is seized quickly and is twisted off its feet by the incoördinated spasms of the muscles. Once down the muscular spasms may be either tetanoid or clonic. In most instances a period of violent paddling, crying and grinding of teeth is followed by tetanic contractions of all muscles. At that moment respiration ceases for a few seconds. The animal then relaxes and may or may not be immediately seized by a repetition of the cycle.

The effect of external stimuli during these convulsions is notable. Sudden noises or handling increase the intensity of the animal's activity. For this reason it would seem wise in practice to maintain quiet around affected animals and to handle them as little as possible.

There is wide variation of malignity in the progress of poisonings. Some animals may become involved in the most unsparing of convulsions, suffer one or several and recover. Others may suffer one convulsion of mild character and die.

In general, differential diagnosis of poisoning by toxaphene is difficult. Toxaphene and chlordane follow similar patterns of involvement but are distinguishable to a degree from DDT. Whereas chlordane and toxaphene produce convulsions, hemorrhages and high temperatures, DDT produces tremors but does not tend to produce hemorrhages or convulsions[4].

As indicated by Radeleff[3] in discussing chlordane, many materials in toxic amounts tend to simulate toxaphene poisoning in some of its phases. Lacking in history, it is not at all unreasonable in many cases to render a diagnosis of peracute pneumonia; in fact, this has been done on several occasions in the field. For this reason a most careful anamnesis is a prerequisite to an accurate diagnosis.

As with chlordane, there is as yet no direct method by which toxaphene may be determined as such in tissues or other material. An approach may be made by determining the excess of organic chlorine in a given sample and multiplying the result by the factor 1.46.

Accurate diagnosis must be based on history, symptoms and gross and minute pathology. Chemical analysis will support a diagnosis but will not necessarily confirm it.

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Clinical Reports

Avian Pneumoencephalitis in Pheasants

That avian pneumoencephalitis may occur in many feathered creatures is exemplified by the occurrence of this condition in a brooder of pheasants.

I was called to examine 600 six-day-old baby pheasants for the Livingston County Sportsman Club. Symptoms shown were those of a respiratory nature—wheezing, gasping, panting. In those showing more advanced symptoms, a nervous condition was noted, characterized by incoördination, grotesque head and neck movements, backward whirling and circling; crooked necks were observed on some birds which were near death.

One hundred of the birds had died each night for the three preceding days. The remainder (about 300) were vaccinated with avian pneumoencephalitis (Newcastle disease) vaccine, each bird receiving 0.5cc injected into the upper leg muscle. The following day 30 more died, after which losses abruptly stopped. Whether the disease had run its course in this brooder of birds or whether the vaccine was entirely responsible for preventing losses after 24 hours is submitted to the immunologists.

These birds came from eggs from a confined flock and not from various selected nests of wild birds.

The unanswered question in this case is the source of infection.

D. M. LIEBENGOOD, D.V.M.

Pontiac, Ill.

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Recovery from Severe Attack of Anaplasmosis

We were called by a dairyman near Chanute, Kansas, to examine a six-year-old Guernsey cow, July 27, 1948.

History—The owner had noticed that the cow was slow and depressed and that she had not eaten for two or three days.

Symptoms—Extreme depression, anorexia, temperature 104°F., mucous membranes and teat pale, milk secretion suspended, blood was thin and showed a very low hemoglobin content.

Diagnosis—Anaplasmosis. This was made on the basis of a microscopic examination of a blood smear in which *Anaplasma marginale* were demonstrated in the erythrocytes.

Treatment—Intravenous administration of 60cc of sodium cacodylate solution (4.5gr per cc) together with 500 cc of 50% dextrose solution initiated the treatment. The owner reported the cow much weaker the following day. At this time three liters (3000cc) of citrated whole blood from two heifers and 500cc more of a 50% dextrose solution were given intravenously. The next day the owner reported the cow too weak to get up. On a subsequent visit the animal was found greatly distressed, groaning with each breath, and giving all the appearances of an unfavorable outcome. One gallon of citrated whole blood (4000cc) which had been collected from a cow that was being slaughtered at the local packinghouse was injected intravenously. When this had been given the animal seemed to feel much better and was able to get up though the breathing was labored. The next day we stopped to see the cow. She was eating nearly normally, and was definitely on the road to recovery. Within a few weeks, milk production was reëstablished. Notwithstanding the explanation given the owner that the cow would remain a carrier of the disease for life, he decided to keep her in the milking string.

Conclusion—The conclusion derived from this case, and several similar cases treated suggests that many anaplasmosis cases which do not respond to ordinary treatment may be saved by massive transfusions of whole blood.

IRWIN DARLING

Manhattan, Kansas

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A test conducted by D. Murnane, B.V.Sc., in Australia, with regular Mastics (Mastin Laboratories) containing 25,000 units of penicillin, showed elimination of infections in eight of nine quarters treated known to be infected with *Streptococcus agalactiae*.

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Erysipelothrix rhusiopathiae infection in mature turkeys has been known in the United States for 15 years. The mortality is high in untreated cases. Swine erysipelas antiserum injected during the incubation period of the disease reduces the losses 50%; penicillin reduces them 90%.

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Rinderpest is the most costly animal disease in the world. It is widespread in Asia and Africa, causing heavy losses in cattle and buffaloes. The death of two million animals annually from rinderpest is considered a very conservative estimate.

Abstracts

Veterinary Uses of Antihistamines

The author reviews the physiology of the various antihistaminics[39], especially those used in France. He then recommends them for the following conditions; acute laminitis, vaccine and serum reactions, dermatoses such as urticaria, photosensitization and eczema. Others are bovine stomatitis, acute coryza and conjunctivitis, and equine anasarca. The antihistamines have been helpful in equine myoglobinuria, dyspneic crises in dogs and horses, and equine periodic ophthalmia. The author feels that the future will show these drugs to be very useful in extensive burns, traumatic injuries, canine and bovine purpura, epistaxis in race-horses, and other nonanaphylactic conditions such as acute pulmonary congestion, and chronic enteritis.—E.B.

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Cancer of the Liver in Cattle[40]

The initial symptoms are a loss of weight and weakness in spite of a good appetite. The milk supply may decrease. The sclera is slightly icteric similar to that seen in recovery from piroplasmosis; the icterus indicates the possibility of an anemia and/or hepatic lesion. Very rarely is there fever. Defecation is decreased. In spite of a normal appetite, stools are scanty, but there is no constipation. The manure is slightly shiny and sometimes discolored but shows no mucus. On rectal examination one feels a doughy, greasy mass which adheres tenaciously to the arm of the examiner. No coarse particles are felt and there seems to be a superdigestion of the food. Retarded peristalsis may be the reason for this, and also the lessened amount of excreta. On autopsy, the cecum and colon are extremely full. The excess fat in the manure is probably due to the diminished bile secretion.

The urine is dark and filled with bile pigments. It is voided frequently and in small amounts. Total volume is not diminished.

Five of the 11 cases had enlarged livers. The liver is not sensitive to palpation or percussion. The kidneys, on the other hand, are extremely enlarged. External appearance in the late stages is marked by emaciation with a dry and motheaten coat. The gait is stiff with the back arched and the abdomen distended. Death usually follows in one to three months. On autopsy, one may find not only the neoplastic tissue in the liver but also necrotic areas which may have ruptured into the peritoneal cavity or reticulum and caused a general or localized peritonitis. Histologically the tumors have been diagnosed as adenomas, sarcofibroadenomas and sarcomas. The enlarged kidneys show disseminated foci of neoplastic emboli, however, these do not account for the marked enlargement of these organs.

Differential diagnosis must rule out catarrhal jaundice which is manifested by anorexia and diminished rumination, and cirrhosis or tuberculosis which are characterized by constipation, then profuse diarrhea and a tense and painful abdomen.—E.B.

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Feline Influenza

Much has been written on the clinical aspects of feline enteritis panleucopenia but relatively little on the respiratory disease referred to here as feline influenza or pneumonia. Authorities in America have also referred to this respiratory disease as feline distemper.[42]

Feline influenza is primarily a disease affecting young cats. An initial rise of temperature which persists for two or three days and then drops almost to normal characterizes the condition with only mild fluctuations throughout its course. A bilateral oculo-nasal discharge due to conjunctivitis and rhinitis is a constant sympton. Affected animals frequently cough and sneeze. Recovery is slow and mortality rate low.

Outstanding laboratory findings that differentiate influenza from feline enteritis (panleucopenia), are those changes observed in the blood picture. The author reports a slight leucocytosis in a few cases but in all a relative neutrophilia.

Sterile filtrates produced symptoms of the naturally occurring condition in injected kittens which confirms early reports (Dalling, 1935, and Baker, 1944) which indicated that the disease was due to a filterable virus.

Postmortem lesions were mainly those of hyperemia and hemorrhage in the lungs. No inclusion bodies were found.

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